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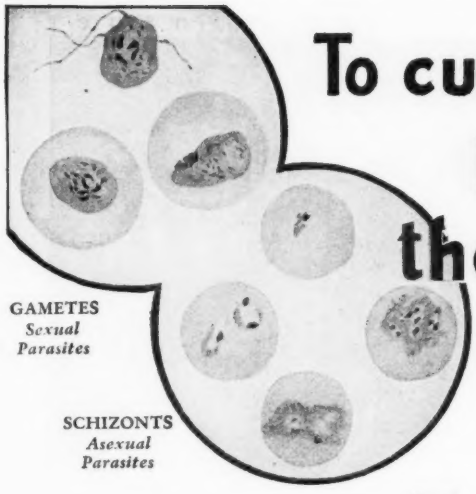

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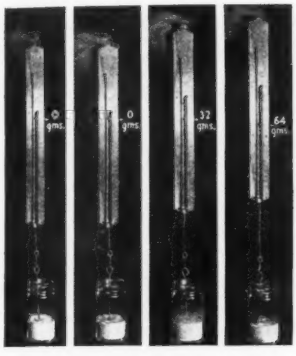

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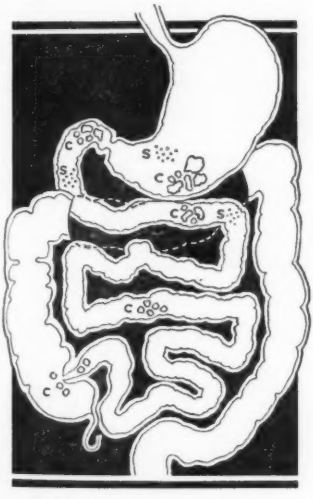

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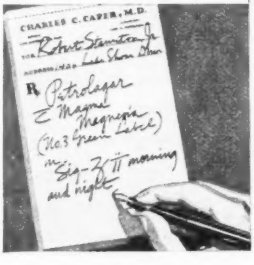

Petrolagar *may be taken just as is . . .*
or

in glass . .

add water . .

stir . .

and drink

"Take two teaspoons Petrolagar morning and night"

Petrolagar with Milk of Magnesia, No. 3 (green label) may be safely prescribed as a harmless aid to bowel movement for growing children.

Petrolagar with Milk of Magnesia, No. 3 (green label) is slightly more laxative than Petrolagar-Plain.

FOR ADULTS: One or two tablespoons night and morning or at mealtime.

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FREE SAMPLE SERVICE TO DOCTORS

MELLIN'S FOOD **4 level tablespoonfuls**
WATER (boiled, then cooled) **16 fluidounces**

for Summer Diarrhea

ACCEPTED AMERICAN MEDICAL ASSN. Correspondence on Foods

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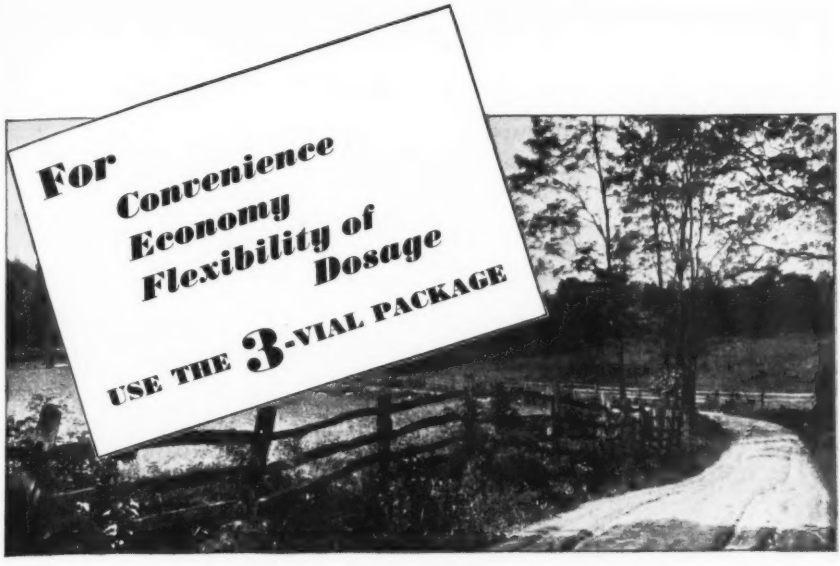
Made from wheat flour, wheat bran, malted barley and bicarbonate of potassium — consisting essentially of maltose, dextrins, proteins and mineral salts.

Further details in relation to this subject are set forth in a pamphlet entitled, "The Feeding of Infants in Diarrhea", and in our book, "Formulas for Infant Feeding". This literature will be sent to physicians upon request.

THE above formula provides a means of supplying the principal fuel utilized in the body for the production of heat and energy and furnishes immediately available nutrition well suited to protect the proteins of the body, to prevent rapid loss of weight, to resist the activity of putrefactive bacteria, and to favor a retention of fluids and salts in the body tissues.

While the condition of the baby will guide the physician in regard to the amount and intervals of feeding, the usual custom is to give one to three ounces every hour or two until the stools lessen in number and improve in character. The food mixture may then be gradually strengthened by substituting one ounce of skimmed milk for one ounce of water until the amount of skimmed milk is equal to the quantity of milk usually employed in normal conditions. Finally the fat of the milk may be gradually replaced, but as milk fat is likely to be digested with much difficulty after an attack of diarrhea it is good judgment to continue to leave out the cream until the baby has fully recovered.

Mellin's Food Company, Boston, Mass.



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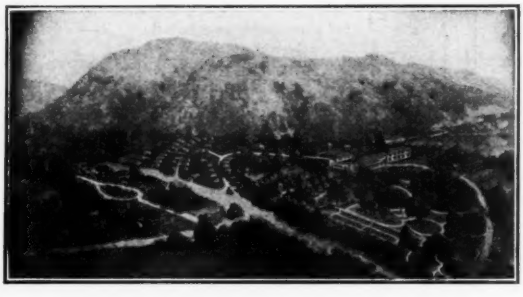

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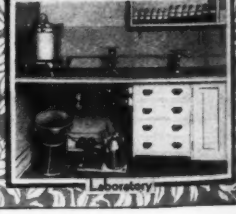

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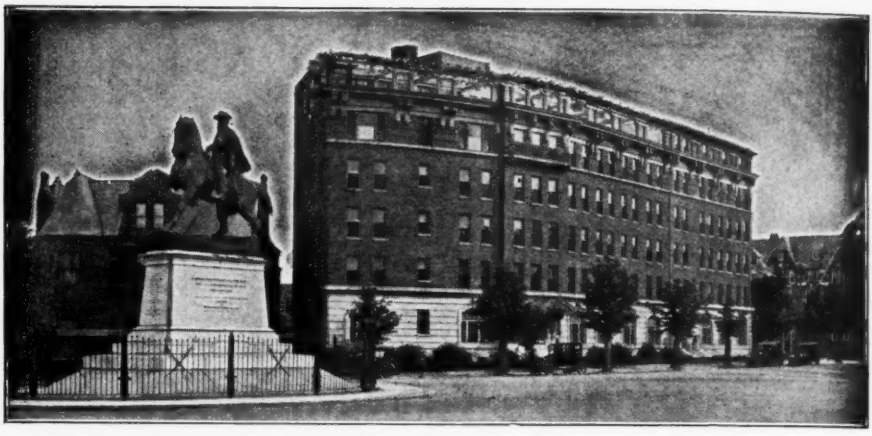

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Stuart N. Michaux, M.D., F.A.C.S.
Charles R. Robins, M.D., F.A.C.S.

Obstetrics:
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Internal Medicine:
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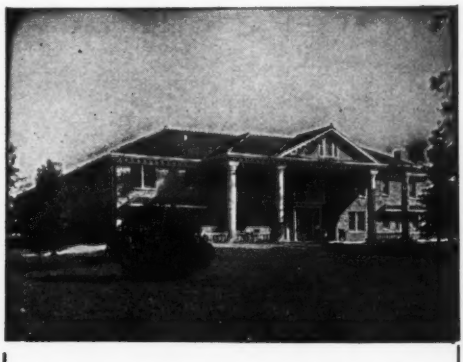

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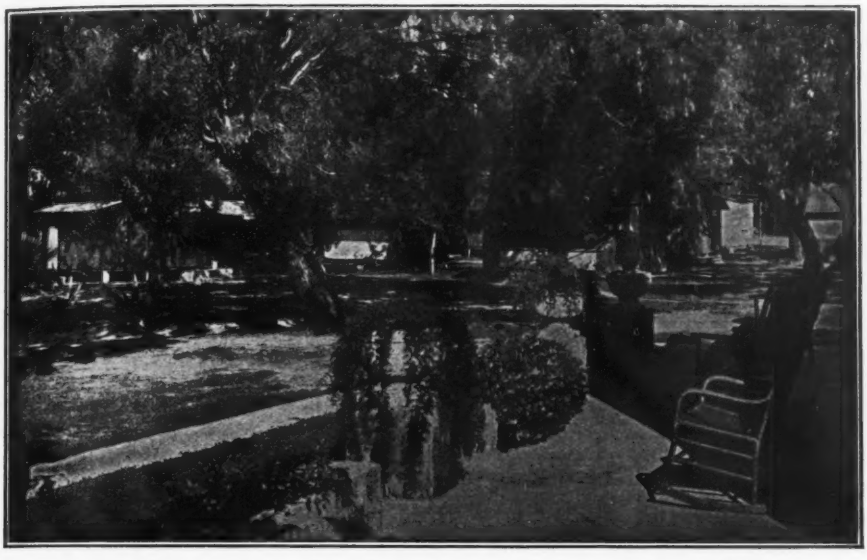

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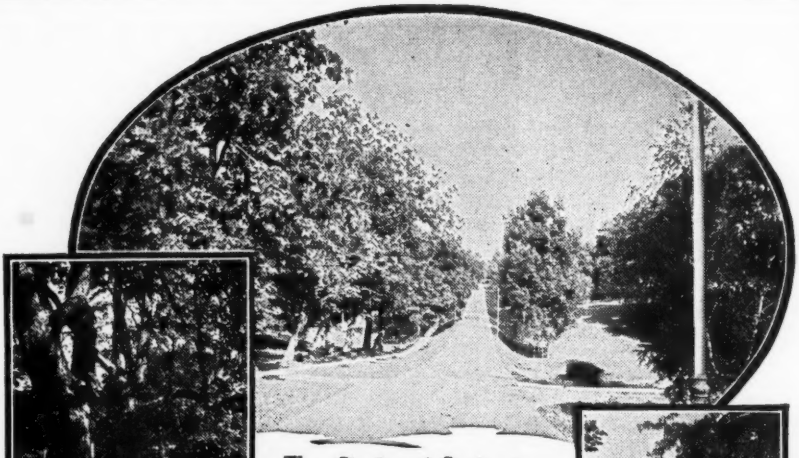

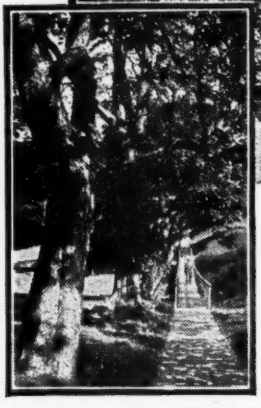

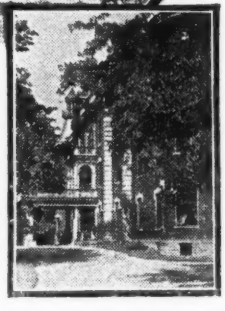

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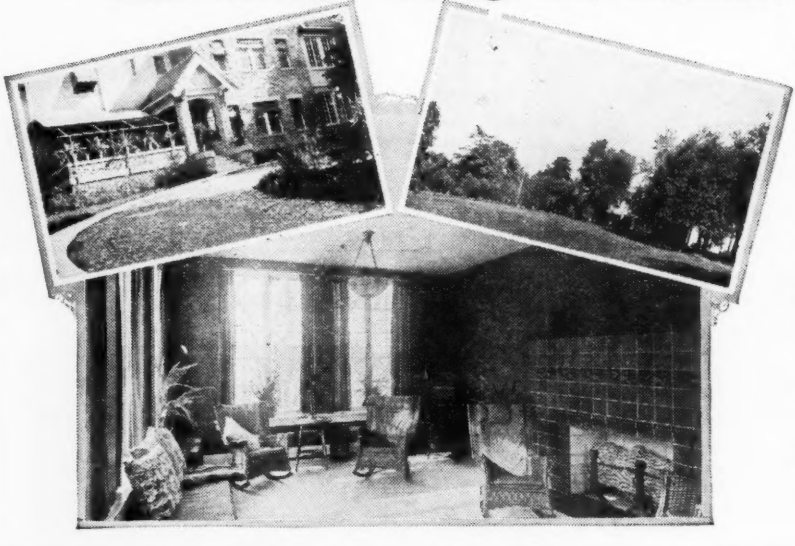

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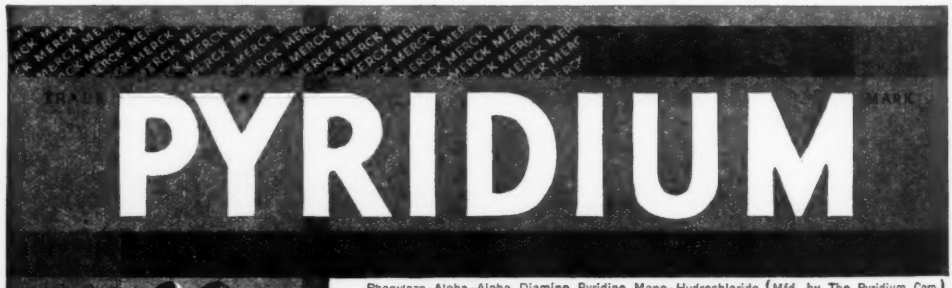

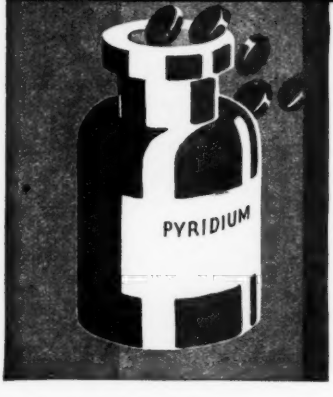

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CANCER OF THE RECTUM: A STUDY OF ONE HUNDRED CASE RECORDS*

By G. V. BRINDLEY, M.D., F.A.C.S.,
Temple, Tex.

Approximately 60 per cent of all intestinal cancers are in the rectum. Carcinoma here, as elsewhere in the body, is a local lesion in the beginning and is amenable to surgical removal with a good prospect of permanent cure. The rectum is not a vital organ and malignancies here permit of wide extirpation. Cancer of the rectum progresses rapidly and in a few months becomes incurable. The average duration of symptoms for the patients with an operable lesion was eight and one-half months. According to statistics, 75 to 85 per cent of the patients with this affliction die of this disease. Due consideration of first symptoms, proper examination, early diagnosis and prompt radical cautery knife excision will materially increase the percentage of permanent cures.

The case records of 100 patients with cancer of the rectum have been reviewed for the preparation of this paper. Carcinoma of the rectum may occur in the young. Two of the 100 patients were under thirty years of age and 12 were under forty. A large majority, 88, had reached, or were beyond, the fourth decade of life. The youngest patient was twenty-three, while the oldest was eighty-four. Males predominated, there being 57 males to 43 females. Three patients of this series were colored. When we give consideration to the location of the growth we find that 17 were considered as recto-sigmoid lesions and 15 others were in the upper rectum. Forty-six were found to be in the ampulla, 18 in the lower rectum, and 4 in the anal portion of the bowel. Therefore, 68 of the lesions were below the peritoneal reflection.

A knowledge of the pathology will prove of value in the study of this subject. A majority of the cancers of the rectum are adenocarcinomata, but occasionally squamous cell epitheliomata are seen. They have their beginning in the mucous membrane as a node of abnormal epithelium and arise frequently from a papilloma or adenoma. Cancer dissemination is in three ways: by direct extension, through the lymphatics, and by the blood stream. Extension through continuity of tissues is the first method of spread and studies made by Dukes would indicate that lymph node metastasis seldom occurs until the lesion has penetrated through the muscular coat of the bowel. Observation in our pathological department would seem to confirm this finding. Our pathologist demonstrated lymph node metastasis in 9 of 41 specimens of rectal cancers studied. In one case of lymph node metastasis the lesion was confined to the mucosa and in two there was a beginning invasion of the muscle, and in six the cancer had penetrated through the bowel wall into the serosa. Rectal cancers are usually very cellular, fungoid growths which tend to early ulceration and bleeding. The ulceration and sloughing of tissue often produce large crater-like lesions with indurated, elevated edges, covered over with exuberant granulations which bleed frequently. This is the type of lesion which is usually seen throughout the rectum, exclusive of the recto-sigmoid and the anus. There is a definite narrowing of the lumen of the rectum in the anal portion and in the recto-sigmoid. The smallest caliber of the colon is at the recto-sigmoid junction. It is in these two parts of the rectum that a more fibrous type of cancer frequently is seen. Epithelioma or squamous cell cancer occurs in the anal portion of the bowel. Scirrhous carcinoma may be found in the recto-sigmoid region. These lesions do not tend so readily to ulceration and bleeding as do the adeno-

*Read in Section on Surgery, Southern Medical Association, Twenty-Fifth Annual Meeting, New Orleans, Louisiana, November 18-20, 1931.

carcinomata, but they are more prone to produce annular lesions with resulting stricture formation. Due to these facts, growths of the recto-sigmoid region and the anal canal can be expected to give rise to symptoms indicative of a narrowing with resulting blocking, more often, and usually earlier, than will lesions elsewhere in the rectum.

Specimens have been obtained for pathological study from 68 patients. Sixty-five of these were adenocarcinomata and three were squamous cell epitheliomata. Nine of the adenocarcinomata were papillary in appearance; one was a mucoid cystadenocarcinoma, another a colloid type, and one was scirrhous cancer. Our pathologist graded these tissues after the method of cell differentiation of Broders. Three specimens were grade I, 29 were grade II, 27 were grade III, and 2 were grade IV. The character of specimens obtained from 4 lesions did not permit of grading. It is seen from a study of these reports that 32 of the 61 cancers graded, or 52 per cent were found to be either grade I or grade II in degree of malignancy and were, therefore, favorable lesions for surgical removal.

Forty-one of the specimens obtained by radical removal of the growth were studied with reference to the depth of penetration of the bowel wall by the cancer and also in regard to the frequency of demonstrable lymph node metastasis. The lesion was found superficial to the muscle in 13 specimens. The muscles were invaded by carcinoma cells in 10 and in 18 the cancer had penetrated through the bowel wall to the serosa. Lymph node metastasis was demonstrated in only 9 of the 41 specimens, or approximately 22 per cent.

It is recognized that the number of specimens studied is too small for definite conclusions. However, when we compare the pathological findings with a study of end results, it appears that there are three factors which materially affect the prognosis in cancer of the rectum. They are: the degree of the malignancy, the depth of penetration of bowel wall by malignant cells, and the presence or absence of glandular involvement. That is, a patient with a high grade cancer with penetration into the bowel wall, and with lymph node metastasis, has but little chance of ultimate cure. Here we would emphasize the fact that the size of the growth alone is a poor index as to its curability.

From the nature of the pathological condition, a rectal cancer at the beginning does not cause a disturbance of function and is practically devoid of symptoms until it has progressed to the stage of ulceration and infection and occasionally until there develops a mild obstruction. Therefore, it is more accurate to say the first symptoms rather than the symptoms of early cancer. The first symptoms of rectal cancer are few and of a mild, incipient, indefinite nature. They are never of an acute, violent degree. This is true of an early malignancy anywhere. The patients with early lesions do not appear very sick and because of this fact it is sometimes hard for them to accept the diagnosis of such a grave condition. The symptoms tend to be of a constant, progressive nature and usually are such that the lesion should be suspected.

Blood in the stool is the most frequent first symptom. Sixty-two of the 100 patients gave a history of the early presence of blood. Twenty-four additional records mentioned the late presence of blood; that is, 86 of the 100 patients gave a history of blood in the stool. Furthermore, "blood in the stool" was given most often as the chief complaint at the time of admission to the hospital. The bleeding is usually in small amounts, but tends to become more frequent and a little more free as the disease progresses. A profuse hemorrhage is quite rare. Notwithstanding the fact that so large a number of patients have blood in the stool, it is seldom that a study of their blood will show a marked anemia. When an anemia is present it is found in patients with advanced lesions accompanied by marked infection and metastasis. The source of the bleeding is frequently mistaken by the patient, he believing that it is from hemorrhoids. Hemorrhoids are often an associated lesion and too frequently the physician also regards them as the source of the bleeding. Thirty-nine patients gave a history of the presence of hemorrhoids and 18 had recently been subjected to a hemorrhoidectomy. This error can be avoided only by always excluding cancer of the rectum before making a diagnosis of hemorrhoids.

Mucus in the stool is of frequent occurrence and is present in the majority of cases. Forty-three patients mentioned the presence of mucus as an early manifestation.

Pain comes next to blood in the frequency of occurrence. Eighty-four of the 100 patients made some complaint of pain. However, early pain is seldom a prominent symptom. Thirty-five gave pain as among the first symptoms, but

an important fact to be remembered is that in only two of these was the pain rather intense at the beginning. The first pain which the patient has is usually described as an uneasiness, a heaviness, a discomfort, a weighty feeling, a soreness, or a mild cramping. This discomfort may become more marked before stool and be somewhat relieved by it. As the disease progresses, the degree of pain is often intensified. However, only 17 of the 100 patients at the time of admission complained of relatively severe pain and 15 of these had advanced lesions. It is only patients with advanced disease that require opiates for relief of pain.

The symptom next in importance and in frequency is some disturbance of bowel function, manifested either by a change in the frequency, the time, the amount or the character of stool. There may appear to be both constipation and diarrhea in the same case. That is, there will be incomplete evacuation associated with frequent, small, liquid stools. Some patients will have alternate periods of constipation and diarrhea. The patient may complain of diarrhea when in fact there is only a frequent desire for stool with but little, if any, evacuation of feces. Constipation and diarrhea are seldom present to a marked degree as an early manifestation of disease unless the lesion be in the recto-sigmoid or the anal canal. Sixty patients gave a history of constipation, 26 giving this complaint as among the first symptoms. Some of these unquestionably were constipated before the beginning of the cancer. Obstruction occasionally occurs in recto-sigmoid cancer without marked preceding symptoms, but complete obstruction is rare even in advanced malignancy of the rectum. There were only three of this series that had practically complete obstruction and two had cancer of the anus, and the other a lesion of the recto-sigmoid.

Diarrhea or a frequent desire for stool was a symptom given by 40 of the patients and it was recorded as an early observation in 17 case records. Sometimes diarrhea is due to medication. Quite frequently the history would state that a laxative, such as mineral oil, had been taken, the objective being to keep the stool soft, which seemed to lessen the degree of pain and to prevent bleeding.

Rectal cancer produces few gastric symptoms, and these are to be found in patients with advanced disease. Only 31 of the 100 even complained of loss of appetite. Weight loss is never a symptom of early disease. Slight weight loss was present late in 34 cases and a rather marked weight loss was a late occurrence of 29 patients. A loss of weight was recorded in 63 case records with an average loss of 19 pounds. A loss of strength may become rather marked in some patients with advanced disease, but it is never a symptom of early lesion.

From an analysis of these histories and a study of early symptoms it is evident that the symptoms of early disease alone are insufficient for making a diagnosis; but they are such that the disease unquestionably should be suspected. Proper examination will confirm the diagnosis.

All patients consulting a physician because of a major complaint should have in their routine physical, a digital examination of the rectum, and every patient with the history of bowel dysfunction, that is, the history of abnormal discharge, or change in the frequency, character, or amount of stool, is entitled to a proctoscopic inspection. All cancers of the rectum can be diagnosed by a digital examination in conjunction with proctoscopic inspection. The x-ray is not essential for making the diagnosis and, furthermore, it cannot be relied upon to make the diagnosis of early lesions. However, the x-ray may be of some value in showing the extent of disease, particularly when the lesion involves the recto-sigmoid. An accurate history of the patient with rectal cancer will cause the condition to be suspected. Then a digital and proctoscopic examination will confirm the diagnosis.

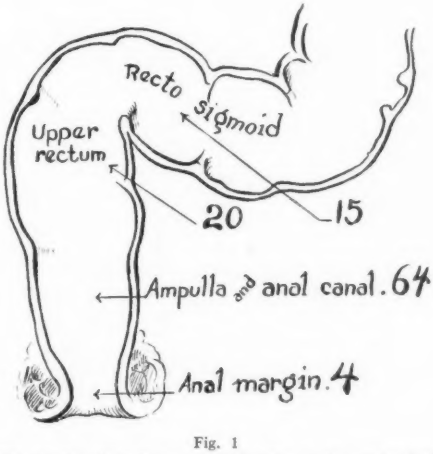

Fig. 1
This drawing shows the respective location of the one hundred cancers.

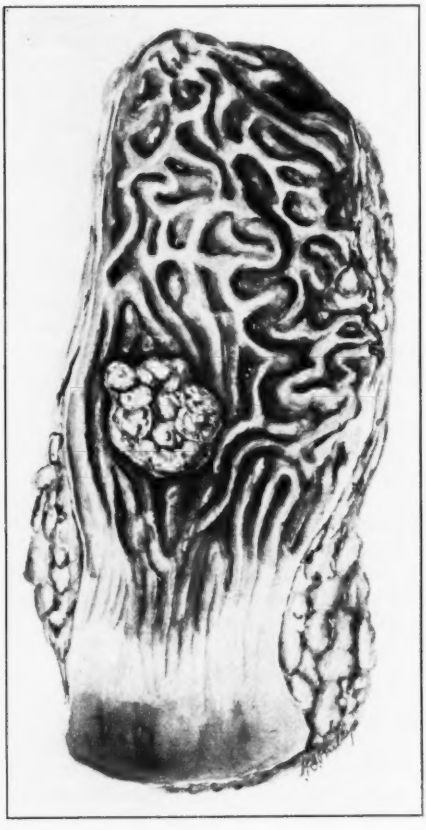

Fig. 2

Early lesion. Patient gave no symptoms of rectal pathology, growth being found when making routine physical examination. Adenocarcinoma, grade II with beginning muscular infiltration without demonstrable lymph gland involvement. Posterior cautery excision more than four years ago. Patient apparently well.

When we study the treatment of these 100 patients, we find that a removal of the growth was performed for 48. Twenty palliative colostomies were done. Twenty-three of the nonoperative group of patients were treated by ray therapy, some with and some without a palliative colostomy. Radium was used alone for the treatment of 7 of this group. Practically all of the patients subjected to a radical removal of growth were given postoperative deep x-ray therapy. Eleven patients declined surgical treatment. This fact should be taken into consideration when considering the percentage of operability and the number of cures.

It is a significant fact that no patient of the 100 obtained an apparent cure excepting by a radical surgical removal of the cancer. Therefore, let us give further study to this group of 48 patients for whom a radical removal of the growth was accomplished. An abdominoperineal excision was performed for 9 patients. An anterior excision was done for 4. One patient, aged seventy-eight, with a malignant papilloma in the upper rectum, had a thorough fulguration of the lesion. A posterior excision without preliminary colostomy was done for 5. A posterior radical cautery excision following a preliminary colostomy was performed for 29 patients.

When we study the end results in this group of 48 patients from whom the cancerous rectum was removed, we find there were three operative deaths, or an operative mortality of 6.1 per cent; two of these patients had combined ab-

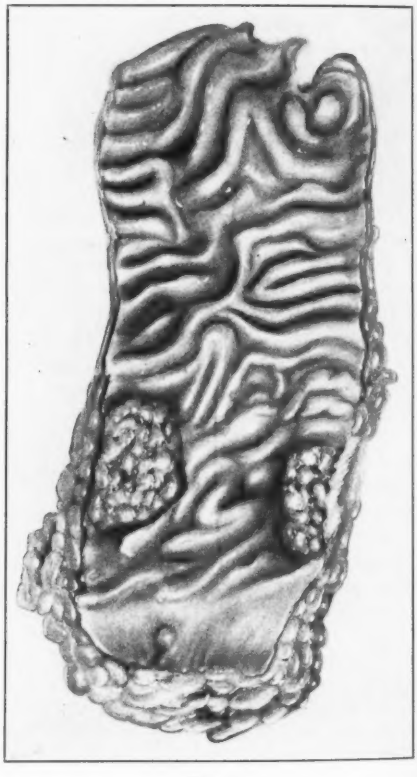

Fig. 3

Small early lesion. Duration of symptoms two and one-half months. Adenocarcinoma, grade II. Muscle coat invaded. No demonstrable involvement of the lymph glands. Posterior cautery excision. Patient apparently well two years later.

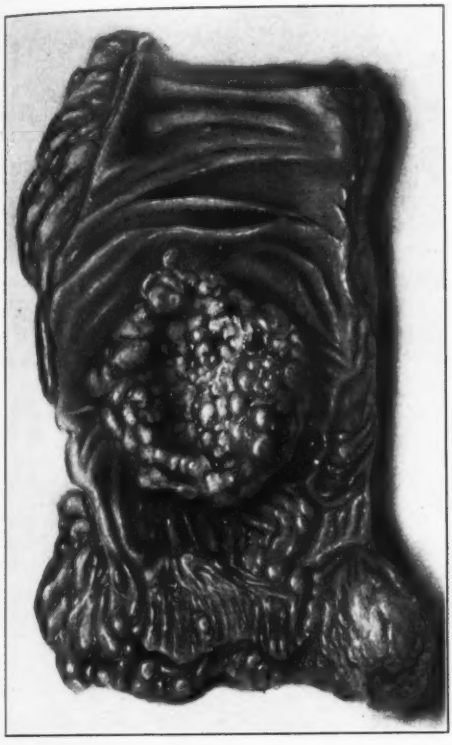

Fig. 4

Moderately advanced lesion. Duration of symptoms five months. Papillary adenocarcinoma, grade III, with invasion of all coats and with demonstrable lymph gland metastasis. Posterior cautery excision. Patient apparently well one year following operation.

dominoperineal excisions and the other a posterior cautery excision. All of the remaining 45 operative cases, except two, have been traced. We find that 14 patients have died since their operations. Three of these deaths are known to have been due to causes other than recurrence of the malignancy. Two died from a circulatory condition, one four, and another six years after operation. The third died a few months after the posterior cautery excision from an acute illness. If we deduct these 3 patients from the 14 known dead, it will leave only 11 that have died following operation apparently from a recurrence of their disease.

Twenty-eight patients have been operated upon approximately three years or more. Twenty-six have been traced. There were three operative deaths in this group. Twelve have died later. However, it is known that three of these deaths were due to intercurrent diseases. Eleven are still alive. Of the 23 traced patients who lived over the operation, 14, or 60.8 per cent, were well three years or longer. Twenty patients have been operated upon less than three years. All have been traced; 18 are alive, and 2 have died apparently from metastasis. There has been no operative mortality within this period.

The percentage of patients accepted for operation, out of all patients seen, will materially affect the operative mortality, the surgical end result and the number of cures. Eleven patients declined surgery, and of the remaining 89, the

Fig. 5

Rather advanced lesion. Duration of symptoms six months. Papillary adenocarcinoma, grade III, with penetration of muscle coats. No demonstrable involvement of lymph glands. Posterior cautery excision. Patient apparently well three years later.

cancerous growth was removed for 48, or approximately 54 per cent of the patients seen who were willing to accept surgery.

DISCUSSION

Cancer of the rectum is not a hopeless disease. Early lesions are local, extirpatable and curable. Lymph node metastasis occurs rather late. Malignant nodes were found in only 40 per cent of excised rectal cancers, as reported by Dukes. Evidence of distant glandular metastasis is frequently absent even in the inoperable cases, as determined by examination when making a palliative colostomy. Liver metastasis is only occasionally found. More patients are inoperable because of local extension to contiguous organs with fixation of the growth than because of metastasis to distant lymph nodes and the liver.

Our experience with radium for the treatment of rectal cancer, particularly with the use of large doses placed in the interstitial and peri-

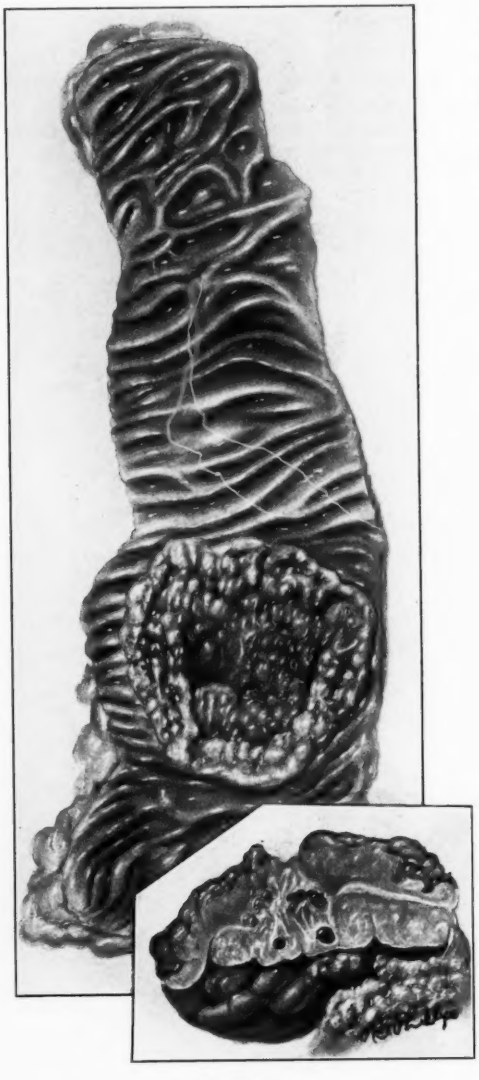

Fig. 6

Advanced lesion. Duration of symptoms six months. Adenocarcinoma, grade III, colloid type. Muscle coats invaded and lymph gland metastasis. Combined two-stage excision. Recurrence a year later.

Fig. 7

Advanced lesion. Duration of symptoms one year. Adenocarcinoma, grade IV, with penetration of all coats and with lymph gland metastasis. Posterior cautery excision. Patient died two years later.

rectal tissues, has been limited; therefore, we hesitate to express an opinion concerning its value. However, we will say that we have regarded radium therapy as a valuable palliative agent and we believe that it may occasionally effect a cure, but it is known that some rectal cancers are much more sensitive to radium than others, and which lesions will respond to radium is indeterminable. Due to the uncertainty of cure by radium, we would reserve it as a palliative agent for the inoperable patient and advise surgical removal for the extirpatable growth.

Radical surgical removal gives to the patient the best chance of permanent cure. Since metastasis to local lymph nodes is found usually only after the growth has penetrated the muscle, and metastasis to distant nodes and the liver occurs quite late, early wide extirpation seems wise and hopeful. Radical excision can be performed with a low operative mortality and will give to some patients a few years of life and to many others a permanent cure.

Many factors influence the treatment of cancer of the rectum and are to be considered in determining operability. The more important of these are the location of the lesion, the extent and fixation of the growth, the probability of glandular and distant metastasis, the degree of the malignancy, and the age, physical build and general resistance of the patient. Again these factors will influence palliation for the inoperable and are to be reckoned with when selecting the type of operation best for a given patient. We would emphasize the fact that all patients should not and cannot be operated upon by the same procedure. The surgeon should be familiar with the various types of operations and methods of approach and should choose the one that will most completely remove the pathological tissues without the patient's assuming an undue hazard.

Cancer in the recto-sigmoid region and upper rectum should usually be removed by a combined abdominoperineal operation, the operation being performed in one or more stages. For a majority of the cancers in the remaining portion of the rectum we would commend, first, a colostomy in the sigmoid, followed later by a radical posterior cautery excision. When the lesion is definitely below the peritoneal reflection a rather wide removal of tissue adjacent to the disease can be obtained by this method, and with a definite increase in the degree of safety over the combined abdominoperineal excision.

The use of the cautery knife for the excision of the malignant bowel has much to commend it. The points of advantage in favor of the general adoption of the cautery for the removal of malignant tissue have been stressed repeatedly in discussions and papers by my senior associate, Dr. A. C. Scott, Sr. The difficulty of excision of the cancerous rectum is not augmented by the use of the cautery knife. A line of cleavage is more readily obtained by it and, therefore, a more accurate dissection can be made. Larger and more advanced growths can be removed with the cautery knife, thereby extending the field of operability. The lymphatics are sealed when severed and, therefore, there is less likelihood of dissemination of the cancer cells. Because of these facts, recurrence is definitely diminished and the frequency and the degree of shock are lessened. The fact that 29 posterior cautery excisions have been performed consecutively with only one operative death would seem to justify the statement that it is a safer procedure than the usual knife excision. The operative mortality for posterior cautery excision was only 3.4 per cent. Three patients operated upon by this method were seventy or more years of age. The ultimate end results are good; for 18 of the 29 patients are still living. Only 6 patients of this group, or 20.6 per cent, apparently have developed a recurrence of their cancer. One of the six is still alive, but has a definite recurrence.

CONCLUSIONS

Several factors can contribute to the cure of more cancers of the rectum. Accurate histories must be taken. Complete physical examinations must be made. Digital and proctoscopic examination must be performed upon all patients with the history of abnormal discharge, bowel dysfunction, or derangement of stool. People must accept the fact that early cancer of the rectum is curable. The patient must be willing to accept a colostomy. Finally, the use of the cautery knife for the excision will contribute to the cure of more patients with cancer of the rectum.

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DISCUSSION (*Abstract*)

Dr. Charles H. Harris, Fort Worth, Tex.—Dr. Brindley's discussion of cancer of the rectum emphasizes the importance of early diagnosis, meticulous preoperative preparation with due consideration to the resistance and the reserve of the patient, and that the operation is done advantageously with the cautery knife. Certainly his report of 26 consecutive sacral excisions of the rectum without a death is most complimentary and reflects the fact of well prepared patients and careful work, such as can only be done by a thoroughly trained organization. His report of 28 rectal cancer operations by sacral excision with evidence of only 9 returning with metastases is certainly a great improvement over any of the reports on carcinoma of the rectum that I have had an opportunity to read. This report is unique in that a high percentage could be operated upon by the perineal route. Such results as these are certainly unanswerable evidence in support of Dr. Brindley's contention of the advantages of cautery excision of carcinoma of the rectum.

There are three different types of carcinoma of the rectum: the adenoid, mucoid, and scirrhous types. The adenocarcinoma or the adenoid type is the most common of them. We should expect to see the squamous cell carcinoma near or encroaching the anal margin. However, the columnar cells undergo some form of change and have all of the appearances of the squamous cells.

Miles, in his report of 1,000 cases, saw 2 cases of melanotic carcinoma with typical malignant endothelial cells and melany. Both of these cases were operated upon by wide excision, and both patients died in twelve months from metastases to other parts of the body. I think that much is going to be done to determine the extent of the operation and the approach by a careful study of the histological cells by Broder's method. There are four grades of carcinoma. Grade one, with a slight tendency to metastasize, will permit a conservative operation and a narrow removal of surrounding structures. Even with metastases near the field as evidenced by adenomatous cells found in the near-by lymphatics, a better prognosis is given by a wider removal. Grade two, which is slightly different from grade one, requires a more extensive removal of the tissues with the possibility of a combined abdominoperineal operation and a wider excision.

Grade three represents a type of more rapid metastases, and we may expect a return in the liver or in a wider spread distribution of malignant cells in foreign parts of the body.

In grade four, whatever the stage of the growth or the operative procedure undertaken, all patients show metastasis and die inside of a three-year period. Possibly this type should be treated by palliative measures, colostomy and radiation in the obstructive case and radiation alone in the non-obstructive case. While the value of this grouping of the malignant cells to determine the prognosis is very promising in its outlook, its evaluation is subject to variations of criticism, and it will have to pass the acid test before its final acceptance by the general profession.

It is difficult to overestimate the importance of early recognition of the many times delusive symptoms of carcinoma of the rectum. Bowel dysfunction is probably the first symptom that is noticed by the patient. In all clinical cases a careful written history should be taken, and those who give a history of bowel dysfunction, evidence of blood, and an unpleasant sensation before and after stool should have a careful digital and proctoscopic examination and x-ray to determine the extent or the advance of the growth, if any. I am much interested in Dr. Brindley's report of his cautery knife excision of cancer of the rectum, and I think that the procedure should inspire a more general use of the method.

Dr. Brindley (closing).—Much good can be done many patients with cancer of the rectum. Statistics given in the paper show a goodly number of three and five year cures. Cancer of the rectum, early, is a local lesion. Lymph node metastasis occurs late. Approximately 50 per cent of rectal cancers are low grade malignancies and, therefore, are favorable lesions for removal.

The cancerous rectum can be radically removed with the cautery with a low operative mortality. Some patients will obtain two to three years or more of palliation and a fair number will be permanently cured. Certainly cancer of the rectum is not to be regarded as always a hopeless disease.

THROMBOPENIC GRANULOCYTOPENIA (AGRANULOCYTOSIS WITH HEMORRHAGES)*

By Roy R. Kracke, M.D.,
Emory University, Ga.

The disease now referred to as agranulocytosis should more properly be named granulocytopenia. This term, as brought out by Harkins,[1] is expressive of the true essential pathology, since it actually designates a decreased number of granular cells, whereas the term, agranulocytosis, refers to an increased number of cells without granules.

Acute granulocytopenia was first described as a clinical entity by Schultz[2] in 1922. However, it existed before that date, as evidenced by Brown's[3] report in 1902. Before Schultz described the condition, however, it was rare, for had it existed in large numbers many years ago, it would surely have been described, because of the ease of diagnosis, definite clinical picture and its dramatic and fatal course.

At this time I have found nearly 350 references to the disease in the medical literature of the world, nearly 500 cases being reported. Most cases are reported from Germany and the United States. Only three reports are in the

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*From the Department of Pathology, Emory University Medical School, Emory University, Ga.

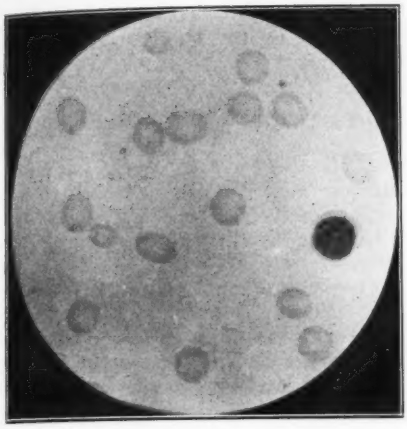

Fig. 1

Peripheral blood in aplastic anemia. Pathology: absence of granulocytes and thrombocytes. The normocytes are very low in number and contain more than normal hemoglobin. Color index above one. Slight anisocytosis, poikilocytosis, and polychromatophilia.

English literature. So, then, the disease seems to have a peculiar geographical distribution.

It occurs chiefly in females and at all ages, ranging from six months to 72 years. I can find no report of its occurrence in a negro unless it be that of Talley and Griffith[4] citing a fatal leucopenia in a mulatto following arsphenamine administration. It has been seen in all classes of life, and in many occupations. It is prevalent in the better class of people, since it is seldom observed in a charity hospital. It is reported as often occurring in nurses and physicians.

Clinically, the disease is characterized by a sudden onset of chilliness, fever, malaise, sore throat, sometimes cervical edema, ulcerations of mucous membranes of the buccal cavity, or about the anus and vagina. An outstanding feature in many cases is the extreme degree of prostration and weakness. Laboratory studies show the granular leucocytes to be almost or completely absent. In true agranulocytosis, the other cell elements are also affected. The patient grows progressively weaker; the white cells fall to a lower level; the lymphocytes and monocytes finally become involved; there is a terminal secondary anemia; and widespread infection is the rule. This infection may be confined to numerous ulcerations, or to a single ulceration, occurring in any part of the body normally inhabited by bacteria. The infecting organisms, usually non-pathogenic under normal conditions, invade the tissues along the gastrointestinal tract and positive blood cultures are usually found. Or the patient may die without showing any evidence of infection and so far as can be determined, may die from a mere absence of neutrophils.

The usual termination is death in the first attack, though the patient may recover, only to be a probable candidate for a later attack. This happens in such a number that one should hesitate for some time before reporting recoveries. There are a few now living who had the disease some years ago, so the prognosis is not absolutely hopeless.

The course of events seems to be well established. The condition should be considered as a clinical entity with a definite cycle of pathological processes, and a well established and easily recognizable clinical picture. The etiology is unknown, but certainly some type of toxic agent attacks the myeloblastic tissue of the bone marrow, this in turn decreasing the output of granulocytes, resulting in loss of the resistance conferred by these cells and in terminal infection of varying severity. It should be noted that when the patient presents himself for medical attention, he is usually in the early stage of the terminal process. Therefore, the clinical findings are most often those of widespread infection and at autopsy evidences of infection are

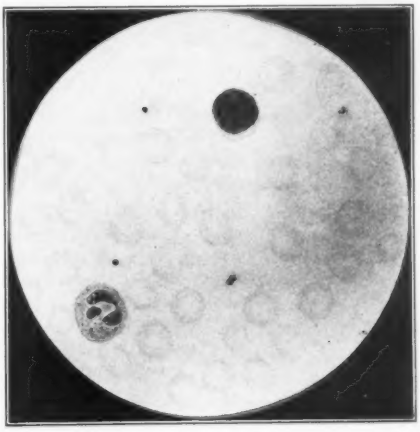

Fig. 2

Peripheral blood in idiopathic thrombocytopenia. Pathology: decreased number of platelets, normal white cell count. Secondary anemia with reduced number of normocytes, low hemoglobin and color index below one. No anisocytosis, poikilocytosis and polychromatophilia.

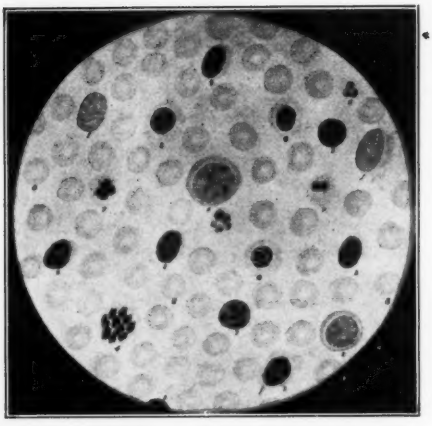

Fig. 3

Bone marrow in acute granulocytopenia (agranulocytosis). 1. Degenerating lymphocytes. 2. Early stages of lymphocytic degeneration. 3. Lymphocytes. 4. Megakaryocyte. 5. Platelet. 6. Megaloblasts. 7. Karyorrhexsis in normoblasts. 8. Normocyte. Pathology: absence of mature and immature granulocytes.

the dominant feature. Roberts and I[5] were able to demonstrate the changes in the blood stream four days prior to the clinical onset by carrying out daily blood counts on one patient for seventy days. I[6] have reported the case of a woman whose granulocytes disappeared prior to the clinical onset of the third attack. On the day preceding the clinical attack, her white cell count was 900 with no neutrophils, though she felt quite well. The next day the attack came and she died two days later. I[7] have recently reported the experimental production of the disease in rabbits by using very small doses of benzene subcutaneously over a long period of time. In this way, this chemical seems to exert a selective action on the myelocytic tissues and leaves undisturbed the erythroblastic and thromboblastic elements. It had been believed formerly that benzene would attack simultaneously all of the bone marrow elements, and this is true when large doses are employed. These rabbits with agranulocytosis often develop terminal ulcerations and blood stream bacterial invasion from organisms already present or introduced organisms, thus following closely the chain of events as it is observed in the human. Also, I have now studied the bone marrow removed from five patients, and the characteristic pathology, that is, an absence of granulocytes and their precursors, is always present. As a result of these observations, I think it may be safely assumed that the disease is primary in the blood-forming tissues of the bone marrow, and that infection is a subsequent but not a necessary part of the picture.

At autopsy the essential pathological bone marrow changes are usually characteristic. The bone marrow is red and not yellow and fatty as in aplastic anemia. It has been referred to as liquefied. Microscopic examinations show the color to be due to a normal amount of erythroblastic tissue and in some instances newly regenerative centers. Some writers have found a definite hyperplasia of the red cell elements. Megakaryocytes are found in normal numbers in uncomplicated cases, the chief pathological finding being a diminution of myeloblastic cells, while adult forms are rarely seen.

This has been the picture in all of the cases that I have studied, with one exception, in which sternal marrow biopsy was made on a man whose white cell count was 500 and whose death was expected daily. The bone marrow, however, showed a large number of granulocytes of varying ages from adult forms through the immature series to the myeloblasts, and could be considered extremely hyperplastic. This was explained when the white cell count rose to 20,000 five days later with recovery of the patient.

It is further evidence that, even though the myelocytic tissue cannot function, it does not, in every case, lose its ability to function. This same recovery of bone marrow activity was also noted in two rabbits in our animal series. In

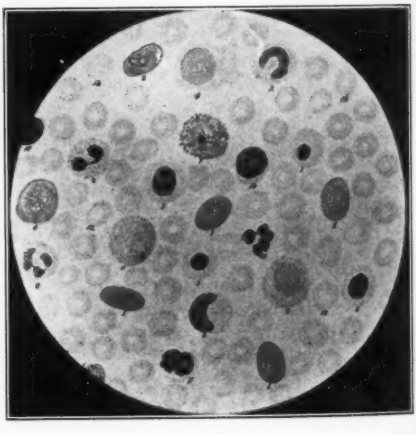

Fig. 4

Bone marrow in chronic granulocytopenia. 1. Degenerated lymphocytes. 2. Band neutrophils. 3. Normoblasts. 4. Early stages degenerating lymphocytes. 5,6, 7. Neutrophilic, eosinophilic, basophilic myelocytes. 8. Segmented neutrophil. 9. Eosinophil. 10. Lymphocytes. 11. Megaloblast showing karyorrhexsis. 12. Normocytes. 13. Thrombocytes.

some instances, notably those patients dying without infection, the post-mortem findings are restricted to the bone marrow changes. A rather common observation is a terminal bronchopneumonia and, in my opinion, a finding of some significance is the presence in almost every autopsied case of hemorrhages in the viscera and under the pleura. This would indicate that, even though no hemorrhagic tendencies are noted in the clinical or laboratory study during life, there must be some deficiency in the clotting mechanism for this to occur regularly.

THROMBOPENIC GRANULOCYTOPENIA

In a disease whose essential pathology lies in a dysfunction of the myeloblastic tissue it seems reasonable to conceive that it would also occur in variable forms, and that other elements of the bone marrow would be involved in some instances. This conception seems well borne out in granulocytopenia, for case reports of the disease complicated with the hemorrhagic diathesis are becoming more frequent. Such instances have been reported by Shea,[8] Hodges,[9] Fisher,[10] Laures and Kenig,[11] Venckunas,[12] and many others. In the field of pediatrics Bigler and Brenneman[13] described the disease in ten children, with a definite clinical picture consisting of gradual onset of weakness, fever, malaise, with a short course and fatal termination, and characterized by petechial and sometimes profuse hemorrhages, marked granulopenia, low platelet count, and reduced red cell count. Their cases might be classified as aplastic anemia, though the children died from hemorrhages and terminal infection.

Since it is becoming more evident that all cases cannot fall within the original diagnostic criteria as outlined by Schultz, a further classification is necessary. For this, I would propose the following:

CLASSIFICATION OF BONE MARROW DYSFUNCTIONS

(1) *Acute Granulocytopenia (Agranulocytosis).*—Involvement of myeloblastic tissue. Marked neutropenia, secondary lymphopenia and monopenia. Thrombocytes and erythrocytes normal.

(2) *Thrombopenic Granulocytopenia.*—Involvement of myeloblastic and thromboblastic tissues. Erythroblastic tissue unaffected. Marked neutropenia, marked thrombocytopenia, normal or slightly affected red cell count.

(3) *Anemic Granulocytopenia.*—Myeloblastic and erythroblastic tissues involved. Megakaryocytes unaffected. Marked neutropenia and erythropenia; normal thrombocytes.

(4) *Aplastic Anemia.*—Myeloblastic, erythroblastic, and thromboblastic tissues affected. Marked neutropenia, erythropenia, and thrombocytopenia.

It is evident that all of these leucopenic diseases, having their essential pathology in the bone marrow, must fall into one of the above classes, and it is true that it is difficult to fix an arbitrary line that separates one from the other. This, however, would be of relative unimportance since treatment would in nowise be different. In thrombopenic granulocytopenia, however, the urgent necessity for accurate study and recognition of this condition becomes apparent when it is considered that the clinical features and laboratory findings are practically identical with idiopathic thrombocytopenia (purpura hemorrhagica), and that in the former, bone marrow stimulation is the necessary therapeusis, and the latter, splenectomy is the accepted treatment.

DIFFERENTIAL DIAGNOSIS

	Thrombopenic Granulocytopenia	*Idiopathic Thrombocytopenia*
Pathology	Bone marrow	Spleen
Red blood cells	Slight secondary anemia	Slight secondary anemia
White blood cells	Marked neutropenia	No neutropenia
Platelets	Marked thrombocytopenia	Marked thrombocytopenia
Bleeding time	Prolonged	Prolonged
Coagulation time	Normal	Normal
Clot retraction	Delayed	Delayed
Blood picture	Color index 1.0	Color index below 1.0
Hemoglobin	Decreased	Greater decrease
Treatment	Bone marrow stimulation	Splenectomy
Prognosis	Poor	Good
Bone marrow	No granulocytes or megakaryocytes	Normal

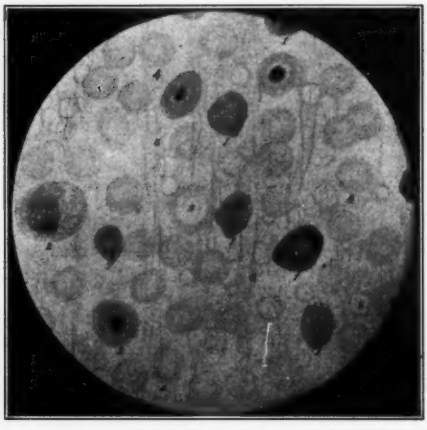

Fig. 5

Bone marrow in thrombopenic granulocytopenia. 1. Degenerated lymphocytes. 2. Myeloblast. 3. Normoblast. 4. Normocytes. 5. Fat globules. 6. Fibrin. Pathology: absence of megakaryocytes and granulocytes. Slight hyperplasia of erythroblasts.

Thrombopenic granulocytopenia is a disease whose essential pathology is an inability of the bone marrow to produce granulocytes and thrombocytes in normal numbers, with the erythroblastic tissues relatively unaffected. The clinical picture is strikingly similar to that of idiopathic thrombocytopenia, in that the patient has weakness, petechial hemorrhages, diminished platelets, normal coagulation and prolonged bleeding time, delayed clot retractility and varying degrees of anemia. The red cell picture is also different, in that the failure of the marrow to produce a normal number seems to disturb the hemoglobin content of each cell very little, whereas the secondary anemia of the terminal stage of purpura is characterized by a greater decrease in the hemoglobin than reduction of cells. Consequently the color index in thrombopenic granulocytopenia approaches or exceeds 1, whereas in purpura it is less than 1.

A study of the sternal bone marrow shows the true pathology and establishes the diagnosis. The marrow is characterized by a diminished number or absence of granulocytes and megakaryocytes, while in purpura the bone marrow picture is normal, or may even show varying degrees of hyperplasia of these elements. In chronic cases showing the hemorrhagic diathesis, I believe a biopsy of the sternal marrow should be made before attempting splenectomy.

The following case, which might be correctly designated as chronic thrombopenic granulocytopenia, is reported to illustrate this condition, and also to show that splenectomy is of no value in a disease whose pathology consists of an inability of the bone marrow to produce granulocytes and thrombocytes.

Case 1.—A white man, pharmacist's mate, U. S. Navy, age 35 years, weight 151 pounds, was admitted to the U. S. Naval Hospital, Washington, D. C., on January 31, 1931. His history was negative prior to January 15, 1931, when he had an attack of influenza, and was in bed three days. During this and following this attack he noticed blood oozing from his gums. He became very weak and exhausted easily with exertion. His physician noticed the pallor and ordered a blood count. The red cells were 2,800,000 and hemoglobin 65.

January 31, 1931, he was admitted to the hospital. His family and past history were essentially negative. Physical examination showed that he was acutely ill, extremely pale. There were hemorrhagic areas on the left tonsil and gums, both thighs, left buttock, back and anus.

Laboratory Findings.—The Kahn was negative, stools contained occult blood, sputum was negative, blood chemistry negative, gastric analysis negative. He had several carious teeth.

Summary of Findings.—(1) anemia, (2) palpable cervical lymph nodes, (3) hemorrhagic skin and mucous membrane, (4) occult blood in stool and gastric contents, (5) achlorhydria, (6) carious teeth, (7) positive tourniquet test, (8) recent influenza, (9) use of Fowler's solution as a mouth spray for Vincent's angina infection about a year ago.

Treatment.—(1) Rest in bed, (2) anti-anemia diet, (3) liver extract, (4) removal of foci of infection, (5) blood transfusions.

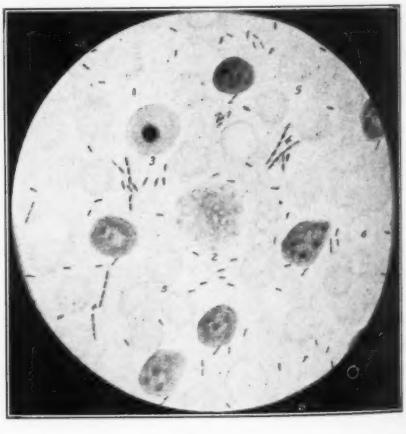

Fig. 6

Bone marrow in thrombopenic granulocytopenia (with fusiform bacilli in the bone marrow). 1. Degenerated lymphocytes. 2. Myeloblast. 3. Megaloblast. 4. Fusiform bacilli. 5. Normocytes. 6. Fat globules. 7. Fibrin.

Date	M. R.B.C.	T. W.B.C.	Per Cent Hemoglobin	Platelets	Reticulocytes	Granulocytes	Lymphocytes	Monocytes	Miscellaneous Tests and Remarks
1-31-31	2.5	3.5	51			43	48	9	Coag. time 3 hrs. 25 min. Fragility test 0.40 to 0.32 per cent
2- 9-31	2.9	3.5	63			49	47	4	Negative malaria
2-16-31	2.2		49						
2-20-31			44	33,600					Coag. time 3 hrs. Bleeding time incomplete, 20 min. Blood transfusion
2-26-31	2.0		48						
2-28-31	2.4		56						
3- 3-31	2.4		63						
3- 5-31	2.3		53						Blood transfusion
3- 7-31	2.8		56						Bleeding continues
3-10-31	2.4		53						Bone marrow biopsy
3-12-31	2.4	3.4	50	35,000		44	54	2	Blood transfusion
3-17-31	2.4	3.4	54	44,000		44	54	2	Diagnosis changed to purpura hemorrhagica
3-20-31	2.3	2.7	46	26,600	0.4				Hair negative for arsenic. Retractibility of clot. Most of the cells settle from plasma without clotting. Only a very small spongy clot formed
3-25-31	2.0	2.7	40	24,000	0.2	35	62	3	Blood transfusion
3-30-31	2.3	2.0	48	30,680	0.5				Bleeding continues
4- 6-31	2.0	2.6	40	18,270	1.1	36	61	3	Bleeding continues. Patient weak and listless
4- 8-31	2.6		48	61,000					Blood transfusion. Consultation. Splenectomy advised. Splenectomy done
4-10-31	2.1	2.9	41	63,000	2.5	62	26	12	Blood transfusion
4-13-31	2.2		46	96,750	2.4				Blood transfusion
4-15-31	2.5	3.9	52	127,000	2.0	64	30	6	
4-17-31	3.2		65	184,320	2.8				Blood transfusion
4-20-31	4.0	4.5	76	171,000	0.8	52	38	10	Uneventful recovery from splenectomy. No bleeding since splenectomy
4-22-31	3.0	5.7	76	115,000	0.8				
4-24-31	3.1		62	80,000	1.2				
4-27-31	4.2	8.2	82	122,000	1.9				
4-29-31	4.2		83	138,000	1.1				
5- 1-31	3.5		78	56,670	0.8				
5- 4-31	4.2		85	88,620	1.7				
5- 6-31	3.7	2.9	75	43,120	1.3	34	62	4	Blood transfusion. Up and about, feeling well. No bleeding
5- 9-31	4.0	3.2	81	65,400		22	75	3	
5-13-31	3.9	4.2	81	98,250	0.6	23	72	5	
5-18-31	3.7	4.5	78	37,200	0.5	28	79	3	Slight oozing from gums. Blood transfusion
5-21-31	4.1	5.6	83	87,000		34	62	4	
5-25-31	3.9	5.7	80	47,000	1.2	16	82	2	Blood transfusion
5-29-31	4.2	5.4	84	92,000	1.6	5	93	2	
6- 4-31	3.9	6.7	79	87,000	0.6	9	87	4	
6-10-31	3.8	6.0	78	54,000	0.8	5	88	7	Blood transfusion Continues to bleed
6-15-31	3.8	5.6	76	68,000	1.2	6	91	3	
6-19-31	3.6	5.9	74	45,000	0.5	4	92	4	
6-24-31	3.8	5.7	81	85,440	0.7	3	93	4	Blood transfusion
6-29-31	3.6	3.8	72	50,900	0.6	4	93	3	Patient worse; bleeding from anus. Purpura spots
7- 3-31	3.2	3.5	65	40,800	0.8	3	95	2	Temperature
7- 8-31	2.9	4.4	59	42,200	0.3	8	90	2	
7-13-31	2.9	4.1	58	41,000	0.2	4	92	4	Patient grows steadily worse. Bleeding in G.I. and G.U. tracts. Large ulcer in upper right mouth, 2.5 cm. in diameter
7-20-31	1.8	2.5	39	18,500	0.4	12	92	6	Blood transfusion (100 c. c.) 7-17-31
7-27-31	0.8	3.3	16			16	84	2	Blood transfusion (100 c. c.) 7-21-31
7-30-31	0.5	3.7	9			12	84	4	Died at 2:00 P. M.

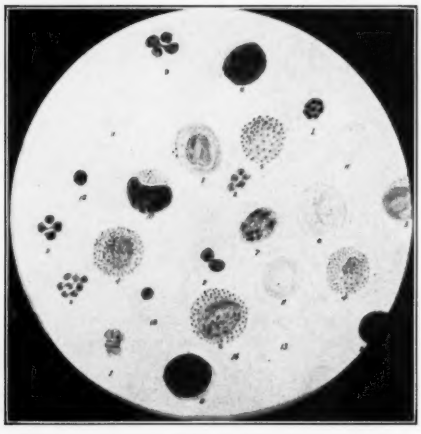

Fig. 7

Bone marrow in idiopathic thrombocytopenia. 1. Megakaryocytes. 2. Thrombocytes. 3, 4, 5. Neutrophilic, eosinophilic, basophilic myelocytes. 6. Myeloblast. 7. Lymphoblast. 8. Lymphocytes. 9. Normoblasts showing karyorrhexsis. 10. Juvenile neutrophil. 11. Normocytes. 12. Normoblasts. 13. Marrow fat space. 14. Marrow reticulum. Essential pathology: slight hyperplasia thrombocytes.

PATHOLOGICAL DIAGNOSIS

(*Autopsy by Dr. Otis Wildman*)

(1) Thrombopenic purpura, atypical idiopathic
(2) Granulocytopenia, idiopathic
(3) Anemia, secondary hemorrhagic
(4) Bronchopneumonia
(5) Splenectomy

Microscopic examination of the bone marrow showed absence of myeloblastic cells, thrombocytes and megakaryocytes, numerous lymphocytes, degenerated forms and hyperplasia of the erythroblastic centers.

Throughout the course of the disease the red blood cells were hyperchromatic with little variation in shape and size, and the color index was usually above one. The picture was quite different from that of secondary anemia in purpura hemorrhagica.

It will be noted that there are many features of this case that apparently justify the diagnosis of purpura hemorrhagica, though when the patient was admitted the diagnosis of aplastic anemia could have well been made. A sternal biopsy was made prior to splenectomy, but in spite of the decreased bone marrow elements, the operation was done in the hope that the removal of the normal agent of thrombocyte destruction might be of value. The correctness of this assumption was borne out by the increased platelet counts after operation. The measure, then, was only palliative, and whether or not it was justified is open to question, since the temporary relief provided is hardly worth the travail of the operation.

The following case illustrates the more acute type of thrombopenic granulocytopenia, and because of its acuteness, severity and short duration, there is little likelihood of confusion with purpura hemorrhagica.

Case 2.—(Patient of Dr. Vernon Powell.) A woman, age 30, was admitted to Emory University Hospital on April 18, 1931. Her chief complaint was sore throat, weakness, and soreness of shoulders, back and legs for the past three weeks. She had begun to feel badly three months before. Her family history and personal history were essentially negative and she was in good health until five months previously, when her Wassermann reaction was strongly positive. Since that time she had been under antiluetic treatment. Three weeks before admission she had a severe ulcerative pharyngitis and peritonsillar abscess, which was incised.

On admission, her temperature was 103, pulse 118, and respirations were 28. She was well developed and well nourished. She had a husky voice and was slightly deaf. There was a macular rash over the abdomen and chest. The right posterior cervical nodes were palpable. The teeth were good. There were no positive chest findings. The throat was red, injected, and had one small ulcer.

The patient continued to have a high, irregular, septic temperature after admission, with multiple petechiae, profuse nasal hemorrhages and ulcerations of the buccal cavity. She finally became irrational, comatose, and died ten days after admission.

Autopsy showed generalized petechiae of the pleural surfaces, gastrointestinal tract and viscera. The bone marrow was hypoplastic for the myeloblastic and thromboblastic elements.

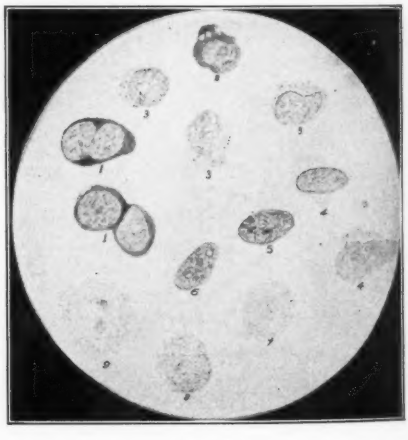

Fig. 8

Marrow lymphocytes in stages of formation and degeneration. 1. Early lymphocytic division. 2. Lymphoblast. 3. Adult lymphocytes. 4. Beginning degeneration with loss of cytoplasm. 5. Degenerated lymphocyte devoid of cytoplasm. 6. Degeneration and rupture of nuclei. 7. Stages of nuclear disintegration.

BLOOD FINDINGS

Date	W.B.C.	R.B.C.	Per Cent Hb.	Platelets	Gran. Cells	Comment
4-17-31	2250		50		2	
4-17-31	2100					
4-18-31	2150	3,000,000	40	40,000	0	Transfusion
4-19-31	700	2,800,000	50		14	
4-19-31	1100	2,770,000	50		8	Blood cultures negative
4-20-31	500	2,960,000	60	60,000	0	
4-20-31	1350	2,540,000	60		4	Petechiae
4-21-31	1500	3,320,000	70		15	Epistaxsis
4-22-31	800	2,900,000	70		4	Ulcerated throat
4-22-31	1050	1,900,000	60		2	Black stools
4-23-31	400	2,740,000	50		3	Bleeding continues
4-23-31	600	2,000,000	50	25,000	0	
4-24-31	750	2,000,000	50		0	Transfusion
4-25-31	400	3,000,000	60		1	
4-26-31	Death this date					

CONCLUSIONS

(1) A brief summary of the important features of granulocytopenia is presented.

(2) A suitable classification for the granulocytopenic diseases, based on bone marrow changes and clinical features, is suggested.

(3) The syndrome of thrombopenic granulocytopenia, consisting of marked neutropenia, marked thrombocytopenia, slight anemia, normal coagulation and prolonged bleeding time, delayed clot retractility, petechiae, hemorrhages, terminal infection, and death, is described, with case reports.

(4) The importance is emphasized of careful differentiation of thrombopenic granulocytopenia, a disease of the bone marrow, and idiopathic thrombocytopenia, a disease presumably of the spleen.

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DISCUSSION (*Abstract*)

Dr. Pauline Williams, Richmond, Va.—The voluminous literature on these so-called blood dyscrasias has appeared within the past few years, most of it since Schultz, in 1922, reported his observations on a group of patients having ulcerated sore throat associated with a leucopenia in which there occurred a marked diminution or absence of the granulocytes and other manifestations which characterize the syndrome called agranulocytosis. Subsequently, the term agranulocytic angina came into use. Later, when cases were observed with similar clinical, blood and bone marrow pathology, but without the angina it seemed apparent that these were simply atypical cases belonging to the same group, which were being erroneously designated. Baldridge and Needles, in a recent issue of the *American Journal of Medical Sciences*, point out that the term agranulocytic angina probably has hindered an understanding of the condition it is used to designate, as it gives unwarranted prominence to an inconstant and non-specific manifestation, namely: the angina. Moreover, the term agranulocytosis may be variously interpreted. Happily, these terms are now being abandoned.

The paper by Drs. Kracke and Roberts, published last year, to which the essayist has just referred, records in detail their findings in a recurring attack of granulocytopenia. This indicates, it seems to me, the most logical approach for future study, namely: the relentless watchfulness for second attacks and the recording of observations between attacks. That the function of the bone marrow is at least temporarily suppressed, and that the granulocytes begin to disappear from the blood stream before the clinical onset, is a most significant finding. This introduces the so-called three onsets, namely: marrow, blood, and clinical, which immediately directs attention to the probability of an initial bone marrow injury. To determine the nature of this injurious agent is only one of the several items to be investigated. Of equal interest is the pathogenesis, especially the answer to the question, "Why the selective aplasia or hypoplasia?"

The importance of differentiating thrombopenic granulocytopenia and idiopathic granulocytopenia cannot be overemphasized, since the therapeutic measures are quite different. Despite the fact that splenectomy has proven effective in cases which seemed to indicate this method of treatment, fatal cases are reported to have followed the procedure, under apparently favorable conditions. It now appears that sternal bone marrow

biopsy is indicated in these dyscrasias where doubt exists as to the diagnosis.

Dr. Jackson and his associates of Boston have described, in the current issue of the *Journal of the American Medical Association*, what promises to be a valuable therapeutic aid in some of these conditions. They treated 20 cases of malignant neutropenia of varied etiology with intravenous and intramuscular injections of a pentose nucleotide, which Dr. Jackson demonstrated in human blood in 1924. This appeared to have a favorable effect in stimulating inactive bone marrow. There were 14 recoveries in the group. The favorable effect, however, seems not to have been noted in cases of leucemia or sepsis without neutropenia and leucopenia.

I cannot take issue with Dr. Kracke, as I agree with him in his interpretations thus far. If his classification is accepted, it will, no doubt, prove most useful.

Dr. Kracke (closing).—I have noticed no evidence of the lymphoid hyperplasia, except in one instance. One of the cases that we have seen in Atlanta was a woman about 30, whose illness was characterized by weakness from a previous attack of influenza. She was so weak that she had remained in bed for three weeks following. However, she suffered no pain. A blood count on this individual showed 8,000 leucocytes, with no granular cells. We felt that we were dealing with an unusual condition, to say the least. We had not encountered it before. Further studies from time to time showed a gradual diminution in these leucocytes until finally the count dropped to 500 or 600 with death. I would interpret this as being some type of a compensatory lymphoid reaction to compensate for a previous disappearance of granulocytes.

Perhaps a somewhat similar condition might have been present in Dr. Owen's case presented this morning, which might have been granulocytopenia with later lymphoid hyperplasia, simulating lymphosarcoma.

POSTOPERATIVE CARE OF FOREIGN BODY IN THE LUNG IN INFANTS AND YOUNG CHILDREN*

By M. F. Arbuckle, M.D., F.A.C.S.,
St. Louis, Mo.

In infants and young children who have aspirated a foreign body, certain problems of treatment occasionally arise which are not often seen in older children. Because of the age of the patient and the size of the airway, the margin of safety is reduced. The postoperative care can, in great measure, be facilitated by a consideration of the findings and in selection of the type of operation. These patients are more liable than older persons to complications, such as shock, cyanosis, dyspnea, and sepsis.

In a robust infant with no complicating condition, the ordinary examination and routine bronchoscopy are indicated. Such patients usually progress to uneventful recovery.

In the case of an infant who enters the hospital in a state of shock with cyanosis and dyspnea, immediate supportive treatment is imperative. Hypodermatic stimulants such as caffein sodium benzoate should be administered, and the patient should at once be placed in an oxygen tent.

A tracheotomy set should be at the bedside and a surgeon should be in constant attendance, pending the completion of arrangements for bronchoscopy. A routine bronchoscopy may then be done with safety; the patient replaced in the oxygen tent and watched for subsequent developments. If signs of sepsis such as fever and leucocytosis develop, with interference with aeration, as indicated by indrawing or stridor, drainage should be provided by a tracheotomy and the very frequent application of suction. This I believe to be the surest method of avoiding serious lung complications.

In the case of the infant who has had a foreign body in the lung for a considerable period and who is septic as the result of lung infection, the probability of exacerbation of all symptoms after operation is great. Such infants are anemic and undernourished and weak and have a lowered power of resistance. The mucosa throughout the tracheobronchial tree is inflamed, and for this reason the airway is already encroached upon. Swelling readily follows the slightest trauma. When the foreign body is removed there is often a flooding of the tracheobronchial tree with purulent pent up secretions. These not only block the passage of air through the trachea, but there is a tendency for the infection to spread to the uninfected lung area, with further exacerbation of symptoms, provided these secretions are allowed to remain in the airway. It is in anticipation of this condition that tracheotomy with lower bronchoscopy is recommended in such cases.

After bronchoscopic removal of the foreign body such patients should be under the constant care of a nurse whose special duty it is to apply suction to the tube whenever, and as often as, secretions are in evidence. Secretions must not be allowed to accumulate in the tube where they will be sucked back and forth with each respiration. The inner tube must be changed and cleansed frequently. Such patients should be in an oxygen tent; fluid should be forced. If suction and change of the inner tube do not

*Read in Section on Ophthalmology and Otolaryngology, Southern Medical Association, Twenty-Fifth Annual Meeting, New Orleans, Louisiana, November 18-20, 1931.

provide sufficient airway, as will be denoted by restlessness, cyanosis and dyspnea, the house surgeon must change the outer tube and, while changing it, he should encourage coughing while the wound is held open by the Trosseau dilator. By this method infants frequently will cough out considerable plugs of mucus, and it has been noted that small particles of foreign body are sometimes coughed out while the wound is thus held open. If by such treatment respiration is not satisfactorily improved, the bronchoscope should be inserted and suction applied. Occasionally plugs of inspissated mucus will be found below the bifurcation; these adhere to the wall of the bronchus and act as foreign bodies. After removal of such a plug there is usually a very considerable increase in the amount of mucus coughed up. This is practically always accompanied by a drop in the temperature, a decrease in the respiratory rate, in the leucocytosis, and an improvement in the general condition.

Inflammatory changes in the bronchial mucosa will, I think, subside more readily if the respiratory rate is slow than when it is rapid. For this reason, as well as the necessity for better oxygenation, the oxygen tent is an important adjunct in treatment.

The question of medication is an important one and is a point about which much discussion revolves. The problem of freeing the airway of secretions must be solved. Is it advisable to administer remedies which will decrease this secretion of the bronchial mucosa, or is this unwise?

Since the secretions of the bronchial mucosa serve as a protective measure because of their bactericidal qualities and mechanically by floating injurious material away from the mucous membrane, the increased secretion of mucus should be encouraged rather than discouraged. Following this line of reasoning, the administration of remedies such as morphine or atropin would be contraindicated, whereas the use of expectorants would be indicated. When the pulmonary mucous membrane pours mucus into the bronchial tubes it will be forced into the trachea, whence it should be removed promptly by suction. If it is allowed to remain, it becomes a frothy, viscid bubbling mass of mucus and pus which fills the airway and also the lung. The astonishing thing to me is that the patient does not more often "drown in his own secretion," a phrase coined by Dr. Jackson, with which you are all so familiar.

As I shall demonstrate by slides, it is rather surprising how quickly the secretions in the tubes become purulent and contain bacteria in astonishing numbers with evidence of phagocytosis. The enormous area exposed to these infectious secretions probably explains the rapidity with which fever, leucocytosis and other signs of inflammation appear. The favorable reaction to tracheotomy and the faithful application of suction and such other methods of treatment as have been described above in this class of cases, justifies, I think, and indicates this method of treatment.

Decannulization may be carried out when the inflammatory reaction has quieted down so that suction is no longer needed.

Case 1.—July 8, 1931, R. S., a three year old boy, three hours before admission, fell with an all-day sucker in his mouth. His mother found him crying and bleeding from the mouth. The candy and stick were intact. He soon became very pale and had a rattling in his breath. When he was admitted to the St. Louis Children's Hospital his mouth and pharynx were filled with bloody, frothy mucus. There was some tracheal stridor. The temperature was 40.3° C., pulse 150, respirations were 40, white blood cells 29,000. Direct examination revealed an enormous quantity of mucus in the mouth and pharynx and loss of the soft tissues down to the vertebral column in the hypopharynx, over an area the size and shape of the candy. The patient was in a state of collapse. The oxygen tent gave little relief. His condition did not improve, and apparently the amount of mucus in the tracheobronchial tree was increasing. It was decided that tracheotomy for drainage might

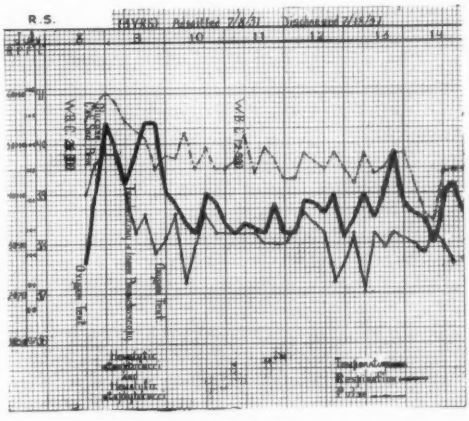


Chart 1, Case 1

Explanations on chart.

At top, reading from left to right: (July 8) W. B. C. 29,000; Glucose, Caf. Sod. Ben. (July 11) W. B. C. 12,900.

At bottom, reading from left to right: (July 8) Oxygen Tent. (July 9) Tracheotomy and lower bronchoscopy. Oxygen Tent. Hemolytic streptococci and hemalytic staphylococci.

Heavy black line = Temperature.

Medium black line connected by round dots = Respiration.

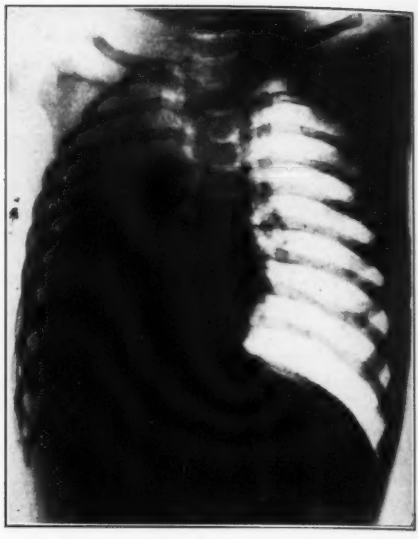
Broken line = Pulse.

help. When the trachea was opened it was found to be filled with thin, purulent secretion. Culture showed hemolytic streptococci and staphylococci.

The cells in the fluid from the trachea were polymorphonuclear neutrophils, many of which contained bacteria. Definite improvement followed tracheotomy. The rales cleared up rather promptly and the temperature of the child improved accordingly. A Hill feeding tube was kept in place for a few days because of the pharyngeal injury.

Case 2.—August 18, 1931, Baby H. E. G., a thirteen months old boy, entered the hospital.

About ten hours before admission he had a sudden violent attack of coughing with marked cyanosis. His color soon improved, but his sleep was restless and he had a rattle in his throat. The parents were reassured by the physician who saw him, and returned home. A few hours later he had another attack of violent coughing with cyanosis. The physician then sent him to the hospital. He arrived in a semi-stupor with the skin dead white and lips purple. There were limitation of chest movements on the right side, dullness, and diminished breast sounds. Fluoroscopic examination showed increased density throughout the right side and very slight movement of the diaphragm on the right. The heart shadow was displaced to the right. The patient was unconscious. A 5 mm. oxygen-carrying suction bronchoscope was introduced, with considerable relief of cyanosis. A rounded white object filled the right main bronchus tightly. There was no forceps space. The object was slippery and it was necessary to bite out a part of its presenting surface in order to make forceps space. The object was grasped and drawn up into the trachea, but the grip of the swollen mucosa dislodged it from the forceps, so that it stopped in the trachea immediately above the bifurcation. Breathing stopped and the patient turned black; the object was pushed back into the right main bronchus so that res-



Case 2, Plate 1

H. G., 8-18-31. Thirty minutes before operation, this antero-posterior view of the chest, supine, was taken. There is complete opacity over the entire right lung field. The heart shadow and mediastinal contents, including the trachea, are displaced into the right chest. There is a small rounded clear area in the upper right chest along the mediastinal side and some of the major bronchi are outlined through the opacity. The left lung field shows an increased air content. The x-ray diagnosis is massive atelectasis of the right lung. The clinical diagnosis is foreign body in right main bronchus.

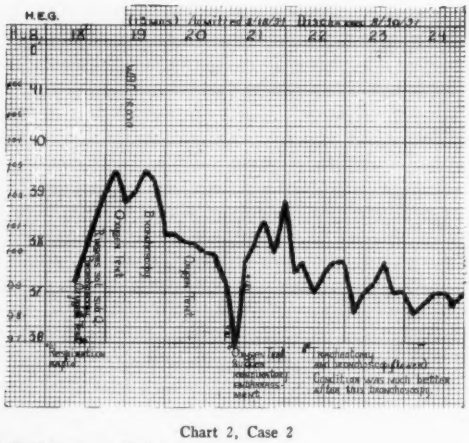
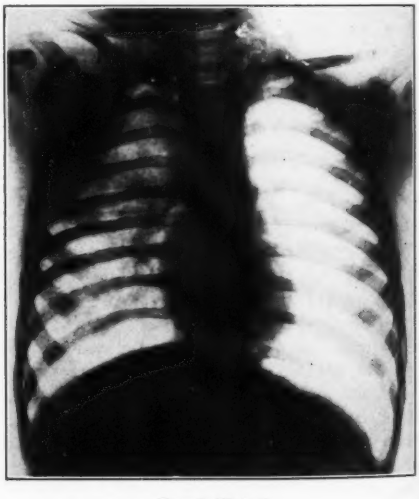


Chart 2, Case 2

Explanations on chart.

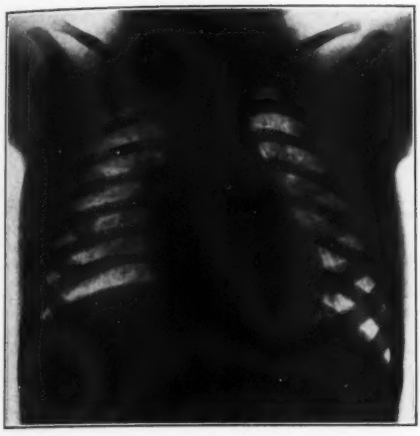
Top: (August 19) W. B. C. 16,050.

At bottom, reading from left to right: (August 18) Oxygen tent—Respiration rapid. Bronchoscopy. Ringer's sol. sub. Q. (August 19) Oxygen Tent. Bronchoscopy. (August 20) Oxygen Tent. (August 21) Oxygen tent—sudden respiratory embarrassment. Tracheotomy and bronchoscopy (lower)—condition was much better after this bronchoscopy.



Case 2, Plate 2

H. G., 8-18-31. Thirty minutes after removal the x-ray film shows partial aeration of right lung with the heart shadow and mediastinal contents, including the trachea, more nearly in normal position.



Case 2, Plate 3

H. G., 8-20-31. The same case two days later shows a normal chest picture.

piration could be carried on in the left lung. A better grasp was then obtained and a large white bean was withdrawn with the bronchoscope. The bronchoscope was then reintroduced and a considerable amount of purulent secretion was removed from both bronchi. No additional foreign body was seen. White cells were 16,050. On the following day the child was in a fairly good condition, but air was not entering the left lung freely because of partial obstruction of the bronchus. A second bronchoscopy revealed a fairly large particle of bean in the left main bronchus. Two days after this, the child developed sudden respiratory embarrassment with retraction and stridor. This was not relieved entirely by the oxygen tent. Tracheotomy and lower bronchoscopy with suction were followed by a marked improvement. Otherwise recovery was uneventful.

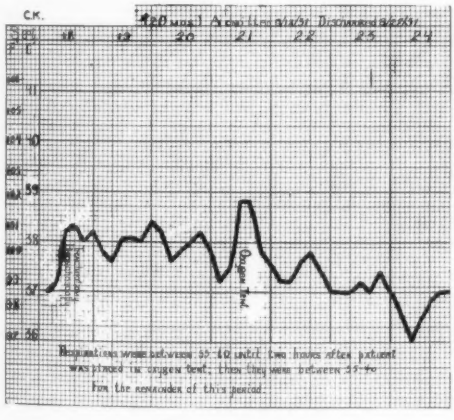

C.K.
Oxygen Tent
Respirations were between 55-60 until two hours after patient was placed in oxygen tent; then they were between 35-40
For the remainder of this period

Chart 3, Case 3

Explanations on chart.

Reading from left to right: (September 18) Bronchoscopy. Tracheotomy. (September 21) Oxygen Tent.

Respirations were between 55-60 until two hours after patient was placed in oxygen tent; then they were between 35-40 for the remainder of this period.

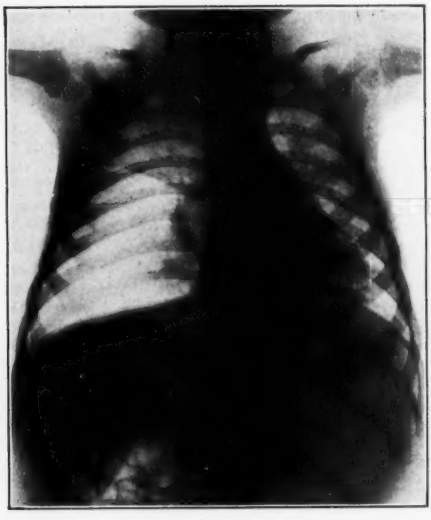
Case 3.—Baby C. K., age twenty months, entered the hospital September 18, 1931.

Five weeks before admission he choked on a glazed peanut. He had an attack of coughing with slight cyanosis. He also developed a wheeze, and this, as well as an intermittent cough and low grade fever, had been present since that time. His temperature was 37.5° C., and white blood cells were 30,000 on admission.

Dr. P. V. Lynch and Dr. W. R. Cleveland, of Evansville, Indiana, had made the diagnosis of foreign body in the lung with atelectasis of the right lower lobe and obstructive emphysema of the right middle and upper lobe. These findings were confirmed by our examination. He had the "split cough." The bronchus contained several fragments of peanut, which were embedded in pus, and there was marked swelling of the mucosa which resembled granulation tissue. The bronchial mucosa everywhere, including that on the left side, was red and swollen. A few hours after removal of the foreign

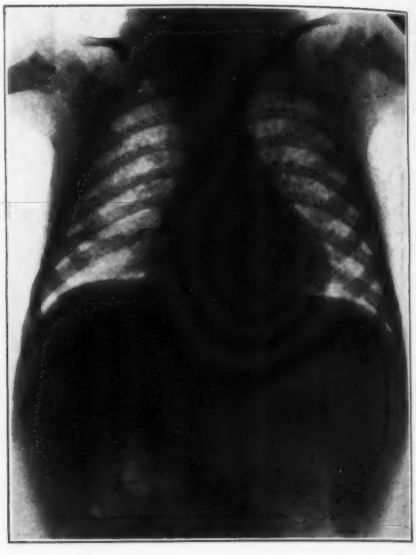
Case 3, Plate 1

C. K., 9-18-31. The plate made at the end of expiration shows displacement of the heart and mediastinal contents to the left and a widening of the lung field from apex to base and from lateral wall to dorsal spine. The right leaf of the diaphragm is depressed. The costophrenic angle is deep and wide; the opposite lung field somewhat narrowed. There is haziness particularly over the upper half of the left lung field, with a moderate increase in the hilus shadow on either side with increased lung markings which extend far out. There is an increased air content in the lower part of the right lung. There is an area of greatly increased density just above the right leaf of the diaphragm and extending from the anterior end of the fifth rib to the anterior end of the seventh rib. X-ray diagnosis is obstructive emphysema of the right lung, with infiltration at the right base. The clinical diagnosis is foreign body in the right main bronchus.



Case 3, Plate 2

C. K., 9-21-31. The plate made at the end of expiration continues to show marked displacement of the mediastinal contents to the left, with marked obstructive emphysema of the middle and lower lobes and flattening of the diaphragm. The infiltration in the base of the right lung is rapidly clearing up as compared with the previous plate.



Case 3, Plate 3

C. K., 9-22-31. The plate made at the end of full expiration shows some evidence of obstructive emphysema in the right lung, but the heart and mediastinal contents are in normal position. It will be noted that there is a marked difference in the position of the heart and mediastinal contents when plates 9-21-31 and 9-22-31 are compared. It will be recalled from the case report that the respiratory rate dropped from 55-60 to 35-40 per minute very promptly after the child was placed in the oxygen tent on 9-21-31, it having been my theory at the time that we would thus in part at least place this lung at rest. (See case report for description of change in physical signs and radiological findings.)

body he was quite restless. There was retraction and the pulse and respiration were rapid. The trachea was opened and found filled with muco-pus. Bronchoscopic suction was applied with immediate improvement. His color was good, but his respiratory rate continued high (55 to 60). The obstructive emphysema was slow in clearing up. It was thought that this might be hastened if the respiratory rate could be decreased. He was placed in an oxygen tent in order to accomplish this. After two hours in the tent the rate dropped to 35 to 40. Within three or four hours the decrease in the emphysema could be made out by the physical signs and corroborated by x-ray plate.

Case 4.—Baby L. P., age twelve months, had aspirated a peanut a few hours before admission, December 9, 1930. On admission she had a moderate cyanosis without marked indrawing, but she was quite restless and her temperature was 102° F. Soon after, she developed stridor. She was seen by some of the other men on the service, who did a tracheotomy and lower bronchoscopy. No foreign body was found. I saw her for the first time on December 11, because of a sudden attack of cyanosis and extreme dyspnea. At this time she looked as if she were about to die. A 4 mm. bronchoscope was introduced through the trachea wound and it was found that the airway contained a very considerable amount of thick tenacious pus. In the right main bronchus there was a plug of pus which had the appearance and consistency of thick glue. This was stuck to the mucosa and was large enough partially to block the lumen. It was removed with forceps. After its removal there was a very considerable amount of pus which welled up from below, and breathing was resumed in this lung. It was necessary to repeat the application of suction through the

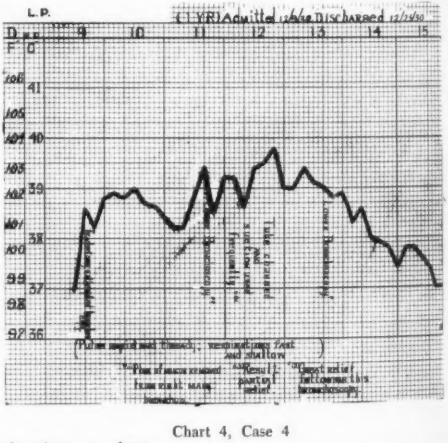


Chart 4, Case 4

Explanations on chart.

Reading from left to right: (December 9) Tracheotomy and attempted bronchoscopy. (December 11) Lower bronchoscopy—plug of mucus removed from right main bronchus. (December 12) Tube changed and suction used frequently—result: partial relief. (December 13) Lower bronchoscopy—great relief following this bronchoscopy.

Pulse rapid and thready; respirations fast and shallow.

bronchoscope several times and suction was applied through the trachea at frequent interva's. Recovery was uneventful.

I am much indebted to Dr. Sherwood Moore and Dr. Hugh Wilson for their help in the radiological study of these cases, and to Dr. Alexis Hartmann and Dr. L. W. Dean for their untiring aid in the clinical study.

SUMMARY

The application of suction through the tracheotomy tube is a most satisfactory method of supplying lung drainage and of freeing the airway of obstruction. If one is unsuccessful by this method, the bronchoscope should be employed, even though it be necessary to do this repeatedly. The secretion of mucus should be encouraged rather than discouraged. This will be aided by the free administration of fluids either by mouth or by parenteral methods. No sedatives should be given. Expectorants are indicated. No drugs should be given which dry up the secretion. The oxygen tent is a most important adjunct, by the use of which many lives will be saved.

DISCUSSION (*Abstract*)

Dr. F. E. LeJeune, New Orleans, La.—The occurrence of edema of the tracheobronchial tree following the aspiration and removal of a foreign body is a condition of greatest concern to both patient and physician. In such edema, cyanosis does not always manifest itself readily and it becomes necessary to place importance upon the symptoms of restlessness and dyspnea. Delay in doing a low tracheotomy after the onset of these symptoms is often regretted.

Following the extraction of a foreign body I have made it a routine procedure to reintroduce the bronchoscope, if necessary, to aspirate the pent-up secretions. Aspiration should not be confined to the bronchus harboring the foreign body, because when the intruder is removed the secretions, as stated by Dr. Arbuckle, frequently invade the other bronchus. Particularly is the procedure urgent and necessary when dealing with foreign bodies of vegetable origin. Nut kernels seem to be the most violent offenders, producing a marked toxic irritation accompanied by a certain amount of edema and great increase in bronchial secretions that cannot be expelled due to impaired laryngeal motility. This condition so closely resembles pneumonia that an error in diagnosis is possible and delay at this stage in doing a tracheotomy is frequently fatal.

I fully agree with Dr. Arbuckle that a low tracheotomy followed by the judicious use of suction is the method of choice in the treatment of edema of the tracheobronchial tree following the extraction of foreign bodies. In these cases the larynx and subglottic space are put at rest and accumulated secretions removed by means of suction if it is used by some one who understands and recognizes the delicacy of the structures involved.

Following the extraction of foreign bodies I have long made it a practice to give these patients small doses of ammonium iodide and syrup of ipecac, an expectorant mixture, to assist them to throw off and cleanse the bronchial tree of the increased secretions. These little patients are always in need of an abundance of oxygen, and I know of no better method to fill this want in cases which develop edema than by the use of the oxygen tent.

Dr. Arthur E. Hoge, Wheeling, W. Va.—In an occasional case in which the mucus is very thick, instilling saline into the tracheotomy tube has seemed to aid in the removal of the secretions. I should like to ask Dr. Arbuckle what he thinks of that procedure.

Dr. John H. Foster, Houston, Tex.—We should draw a line of distinction in these cases between edema of the lungs and purulent bronchitis. They are two distinct types of case. Personally, I think as a preventive, or as a treatment in the early stages of the edema of the lungs, there is nothing so good as atropin. It prevents an excessive amount of secretion which forms hard masses in the lungs if allowed to remain there, it prevents atelectasis, and I feel that the use of atropin is thoroughly indicated in these cases. After purulent bronchitis with thick secretions has developed, then I think atropin should not be used.

When the secretion has become thick, with a tendency to form hard masses in the bronchial tubes and block them, nothing will help except suction, and even later tracheotomy; but until that condition supervenes I would not, unless there is an edema in the glottis, see any indication for tracheotomy. Certainly it is true, as Dr. Jackson pointed out years ago, that whenever you do a tracheotomy you remove Nature's greatest aid in expelling things from the bronchial tubes. In other words, in order for a patient to cough well it is necessary to have a glottis to close, giving pressure and an explosive action. When you put in a tracheotomy tube that is lost.

Dr. George B. Collier, New Orleans, La.—I want to ask Dr. Arbuckle if he uses local anesthesia or general for his bronchoscopy?

Does he employ, when taking out the bronchoscope, something like mono-chloro phenol, instilling it into the bronchoscope as it is removed?

Does he think it would be advantageous to use, for example, compound tincture of benzoin, as we use it in croup?

Dr. Louis Daily, Houston, Tex.—In serious cases we may have to resort to tracheotomy to save life, but this is not the rule.

The possibility of two foreign bodies, one of which may not be radiopaque, should not be forgotten.

Dr. H. M. Taylor, Jacksonville, Fla.—When a patient comes in with subglottic edema, before I do a bronchoscopy, I try to decide whether I may have to do a tracheotomy in three or four hours following the bronchoscopy. If one has to do a tracheotomy, I think it is better to do it first.

Dr. T. W. Moore, Huntington, W. Va.—We are often misled by the history in foreign body cases. Even when it is perfectly clear, the parents will frequently insist that the child could not possibly have put a foreign body into its mouth.

Dr. William A. Wagner, New Orleans, La.—I do not employ early tracheotomy in edema of the bronchial tree unless there is edema of the larynx. A functioning larynx is necessary for efficient removal of accu-

mulations in the trachea. I prefer frequent bronchoscopy and in addition I believe in dependent drainage by lowering the head of the bed with the administration of ammonium chloride or any other expectorant in the early stage, and the use of atropine in the asthmatic stage. I think we have overlooked the use of digitalis to maintain a strong heart. In addition to the suggestions of the essayist, I prefer frequent bronchoscopy, dependent drainage, and supportive measures for the heart.

Dr. Arbuckle (*closing*).—I have long ago come to the conclusion that trauma is not the sole cause of the edema of the larynx which occurs in these cases. They are already infected, and trauma which ordinarily would pass unnoticed may cause an unusual amount of swelling.

I do not give drugs if I can avoid it except expectorants, which are practically always indicated.

We usually re-examine these small children immediately after operation, using a smaller tube than was employed during removal of the foreign body. If I use a 5 for operating, I use a 4 for re-examining, which causes very little trauma. This procedure gives an opportunity to remove by suction secretions present in the tracheobronchial tree, and it is surprising how rapidly the tubes fill up. Occasionally an additional foreign body is found.

I am not over enthusiastic about the instillation of watery solutions into the bronchial tree. I know it is done, but I prefer to have the needed moisture come from the blood stream plus steam inhalation either with or without the addition of compound tincture of benzoin.

Dr. Foster mentioned the formation of hard masses of mucus in the lung. If the mucus does remain in the lung for a long period, it will surely form hard masses, and the only way to prevent this is to keep the secretions in a fluid state and remove them by suction. The use of compound tincture of benzoin in steam has helped in many cases.

The great importance of withholding drugs which decrease the secretion of mucus and check the impulse to cough is, it seems to me, self-evident.

I do not use anesthetics of any type in young children. They frequently are already using the accessory muscles of respiration, and if you put these out of commission by anesthesia, artificial respiration will be required.

In young infants who are already unconscious their best interests are served by doing a tracheotomy first, then a lower bronchoscopy. A bronchoscope in the trachea is a great comfort to the man doing the tracheotomy under such conditions.

Undoubtedly it is true that greater intrabronchial pressure and a more thorough going cough can be produced if the larynx is functioning normally, but the fact remains that patients do cough with very considerable force through a bronchoscope and even through a tracheal tube. One point which I especially wish to emphasize is the fact that infants and very young children do not cough things out of the larynx well, even liquids, so that the larynx soon becomes filled with mucus which resembles whipped cream in consistency.

Dr. Wagner spoke of the indications for tracheotomy and advocated late tracheotomy. With all deference to Dr. Wagner, my experience is, and I think it is the experience of every man who has done a great number of these cases, that more lives are lost by late tracheotomy than by any other condition with which these patients are confronted. This is one of the points with which Dr. Chevalier Jackson deals at length and on the importance of which he lays special emphasis.

A METHOD OF INCREASING THE SPECIFIC RESISTANCE OF A SYPHILITIC INDIVIDUAL TO HIS DISEASE*

By CHARLES C. DENNIE, M.D.,
Kansas City, Mo.

Jean De Vigo recommended mercury in the treatment of syphilis in the late part of the Fifteenth Century. Francisco Lopez De Villalobos discarded it in 1498, because he thought it was injurious to his patients. For four centuries this metal was used to combat this universal disease. It was employed in every conceivable form. It was given by mouth, as inunctions, injections, inhalations and even in the vein. The original plasters of Jean De Vigo were probably as effective as the more modern methods of administration. In all these four hundred years the only effective divergence from the mercurial course was the administration of the iodide recommended by Lugol. And then came the astounding discovery of Ehrlich in the early part of this century, which more than any one thing stimulated the study of this disease. A decade later, bismuth was employed by Levaditi and tryparsamide used by Lorenz *et al* in the treatment of paresis.

The chemical treatment of syphilis has changed but little during the last twenty years, nor has its effectiveness been much increased. True, the different therapeutic agents have been juggled about and the syphilographers have found out what to do with them and what not to do with them, but the basic principles of treatment have remained the same. We do not, as yet, know a successful treatment for syphilis. We are at present in the calm of our own complacency. Because we employ a drug that drives away cutaneous eruptions, causes mucous patches to disappear and temporarily restores the mental function of a paretic, we are satisfied. We must admit that a satisfactory cure of syphilis has not been devised or even approached. Therefore, we must use to the best

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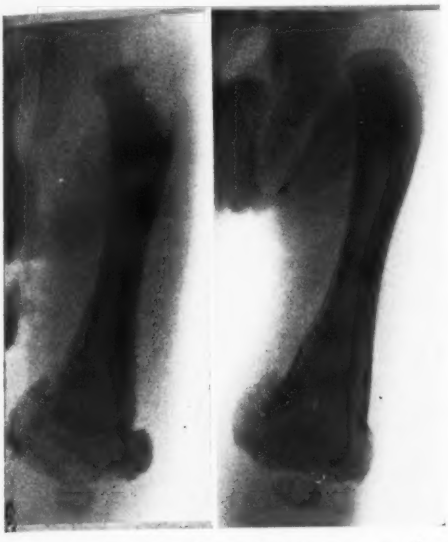

Fig. 1, Left.—Shows radiographic studies of the femur of a three months old infant taken before malarial treatment was administered. It will be noted that the great trochanter is entirely destroyed, while the distal end of the bone shows a productive process.

Fig. 2, Right.—Shows the same bone four weeks after malarial therapy has been instituted, that is, four weeks after the first chill. It will be noted the trochanter has been restored and that the distal end of the bone shows a diminution of the productive process. It is evident that the malaria had a double action, stimulating the osteoblasts at one end of the bone and retarding the osteoclasts at the other end of the bone.

of our advantage those things that we have at hand. Nearly all of our energy has been directed toward finding a remedy that will kill the spirochete, the cause of the disease, and very little toward bettering the condition of the individual who has within his tissues these same organisms. The non-specific treatment of syphilis has been attempted for many years, but it remained for Wagner von Jauregg to clarify the muddled waters and establish this proposition upon a sound therapeutic basis. Malaria has been used long enough and successfully enough to take it from the field of experimental medicine and place it upon an equal footing with the best of our therapeutic agents.

The arsenicals, mercury, bismuth and the iodides are on one side of the therapeutic scale, malaria and the foreign proteids on the other. The former are used to kill, if possible, the invading organism; the latter to raise the resistance of the individual to his own disease. One complements the other, so that the successful treatment of the individual demands the employment of both. Most therapeutists bend their efforts toward killing the offending organism and pay too little attention to the individual who has the disease.

THE ACTION OF THE MALARIAL PARASITE IN THE HUMAN ORGANISM

The defense of the body against syphilis probably lies in the recticulo-endothelial system. The pathologist recognizes this fact when he examines syphilitic tissue under the microscope. The collar of lymphocytes in the perivascular tissues, the thickening of the endothelial lining of the blood vessels, the propagation of the stellate Kupffer cells in the liver which can be found in any stage of syphilis, are but indications of the battle that the reticulo-endothelial system is waging against the *Spirocheta pallida*. If this battle is successful, the individual lives in comparative health. If it is unsuccessful, the host either dies or is crippled for the rest of his life, but in most instances an armed truce is set up between the host and the parasite, which may be broken at any time. In a long battle of many years, the reticulo-endothelial system be-

Fig. 3, Left.—Shows a mushrooming of the distal end of the femur with a deposition of excess bone around the joint, thus resembling a Charcot's joint.

Fig. 4, Right.—The same joint four weeks after malarial therapy had been instituted showing a shrinking of the distal end of the femur and a disappearance of the small bone fragments.

Fig. 5, Left.—Shows a disappearance of the lime salts from both ends of the tibia and fibula.

Fig. 6, Right.—Shows a replacement of the lime salts after malarial therapy.

comes sluggish in its action against the invader and no longer carries forward the fight as it did in the beginning of its warfare. It is at this time that the immunity of the individual must be raised to the specific disease.

It has long been observed that certain types of syphilis do not respond to the ordinary methods of treatment. Again, this disease may respond well at first and later revive and continue in spite of all therapeutic efforts. In these cases the immunity of the individual toward his disease must be increased.

Let us state, as the basis of this thesis, that malaria does not free the individual of his disease, but so increases his specific resistance that subsequent treatment by ordinary means becomes much more effective. This increased resistance is so marked that the individual will respond with alacrity to the same treatment that was found to have no beneficial action before the malarial regime was instituted.

The plasmodium of malaria is perhaps the most powerful stimulator of the reticulo-endothelial system known to medicine today. To the excellent work of Bahr and Breutsch we are indebted for the theory of its action. Breutsch drew his conclusions from the histological examination of a great mass of material gathered over a period of years.

The first action of the parasite is the stimulation of the endothelial lining of the smaller blood vessels with the consequent enlargement and desquamation of the individual cells composing that lining. These cells then take up an independent existence with the power of capturing, devouring and digesting their own food. It is observed that macrophages thus formed often contain from one to three red blood cells containing the malarial plasmodium in all stages of digestion. The large reticular mononuclears found in the blood of the malarial patient are probably specimens of this same macrophage.

It is assumed that the *Spirocheta pallida* is devoured in the same way. The stellate Kupffer cells, derived from the reticulo-endothelial system, and found in the liver and spleen, are increased in number and activity.

The plasmocytes and lymphocytes, the second and third line of bodily defense, are increased in number and take up a certain amount of activity. The wandering cells of reticulo-endothelial origin, brought into existence because of the chronic irritative activity of the *Spirocheta pallida,* are stimulated into greater activity because of the action of the malarial parasite. All have the presumptive power of accomplishing the following feats:

(a) Using the malarial parasite as food.

Fig. 7, Top.—A case of interstitial keratitis in a seven years old boy confined to one eye, the left.

Fig. 8, Bottom.—The same boy four weeks after his first chill induced by malarial inoculation.

Fig. 9
Ulcerative syphilis of the skin extremely resistant to all the ordinary methods of treatment. (From Dennie in the American Journal of Syphilis.)

(b) Destroying the *Spirocheta pallida* in the same manner.

(c) Using as food injured cells, cell detritus and immature cells blocking lymph channels or interfering with the activity of vital cells.

(d) Restoring to the reticulo-endothelial system its original strength.

This desirable result is probably brought about because of the power of these wandering cells to penetrate deep into tissues where the blood supply is not overabundant, and their ability as ameboid bodies of insinuating themselves between cell units. The paretic responds because these cannibalistic units can penetrate into territory that ordinary antisyphilitic remedies cannot reach, thus destroying great numbers of the spirochetes present in that region. More important is the fact that these same units carry away destroying toxins, injured cells and the great mass of detritus left in the wake of the invading syphilitic parasite. The comparatively healthy, but momentarily slowed brain cells are allowed to recover because of the fresh influx of oxygenized serum brought to them through cleared lymph channels.

The role of the fever in this complex problem is the bone of contention. The majority hold that excess temperature is the greatest factor in the production of favorable results. By what means it is brought about is a matter of conjecture, one school claiming that the organism of syphilis dies when the temperature rises above a certain point, another asserting that the excessive oxygenation of the tissues is responsible because of the anaerobic character of the *Spirocheta pallida*. Both schools may be right, but it is the opinion of Breutsch that high temperature is an activating factor only. He believes that the macrophage is highly indifferent to the *Spirocheta pallida* at normal body temperature. As the temperature is raised the macrophage becomes more voracious in direct proportion to the height of the fever. Some weight is added to this theory by the use of diathermy.

We know that syphilis is first an acute stimulator of the reticulo-endothelial system, and as the tissues become used to the presence of the syphilitic parasite, it is converted into a chronic source of excitation. Therefore, there are always present a certain varying number of macrophages, plasmocytes and lymphocytes. When one raises the temperature of the syphilitic, these wandering cells take on renewed activity and not only destroy a great number of parasites, but remove a varying quantity of dead material that interferes with the oxygenation and nutrition of the living cells. But we do not believe that heat alone will cause the production of new macrophagic units. Therefore, temperature alone cannot be the main factor. The diathermists, in order to prove their con-

Fig. 10
The same case four months after malarial therapy had been instituted. (From Dennie in American Journal of Syphilis.)

tention, must show that temperature is capable of producing new macrophagic units.

All of our knowledge of the action of the malarial plasmodium has been drawn from the action of this parasite upon the paretic. Simple deduction leads us to believe that this action would not be specific for paresis alone. The same phenomenon should take place in constructive bone and joint lesions, in resistant skin manifestations, in interstitial keratitis and in enlarged liver and spleen; in fact, in any location where the syphilitic lesion has not passed beyond the stage of resolution. To anticipate that mature connective tissue could be removed would be absurd.

BONE AND JOINT LESIONS

Only proven cases of untreated syphilis were used for this experiment.

In the radiographic and photographic studies each group is represented by a single case. This does not represent the entire number of cases treated by the malarial method.

From these three distinctive cases we will attempt to gain some knowledge.

It has been our observation that constructive syphilitic lesions will resolve under malarial therapy. Destructive bone lesions of recent origin will be repaired under the same regime.

Interstitial keratitis will clear up, but will recur unless subsequent antisyphilitic treatment is instituted.

Resistant skin lesions will heal under malarial therapy, but will recur unless antisyphilitic treatment is immediately instituted.

Wassermann negative resistant cases with cutaneous skin manifestations may become Wassermann positive following malarial inoculation.

From the observation of this experimental data we surmise that malarial therapy does not act at all in the same way as does the treatment with the arsphenamines, mercury and bismuth.

It is a well known fact that spirochetes cannot be found in active lesions forty-eight hours after proper treatment with the arsphenamines. This signifies that the arsenicals, in combination with some substance of protoplasmic origin, destroy the *Spirocheta pallida* by direct action. Bismuth and mercury probably act in the same way, but are slower in their action. We would then designate these substances as direct actors, although they might have a side action on the reticulo-endothelial system.

The action of the malarial plasmodium setting into motion the reticulo-endothelial system is much slower in destroying the parasite of syphilis. This phenomenon must be designated as an indirect action. The destructive action against the spirochete is due to the increased activity of the host.

We can answer, once for all, a matter of dispute that has been in debate for a long time.

Should patients receive antisyphilitic treatment after the use of malarial therapy? The answer is decidedly, yes.

As soon as the individual has recovered from the effects of his malaria, he should receive energetic treatment with the arsphenamines, mercury, bismuth and the iodides, unless there are contraindications for the same. This is true whether the patient is a paretic, a tabetic or has some form of somatic syphilis.

CONCLUSION

The arsphenamines, mercury and bismuth, modified by some protoplasmic body substance, have a direct action upon the *Spirocheta pallida*. When one uses these drugs, he is attempting to destroy the cause of the disease.

Malarial plasmodium stimulates the reticulo-endothelial system and thus raises the resistance of the individual to his disease. With this agent, one treats the individual so that he may hold the disease in check.

DISCUSSION (*Abstract*)

Dr. Thomas W. Murrell, Richmond, Va.—Dr. Dennie says that he is not advising a method of therapy for syphilis, but is attempting to prove that there is something besides the bactericidal action of drugs which may be employed. To me the key to the whole situation was his last slide. This man, inadequately treated by antisyphilitic measures, still had exaggerated syphilitic skin lesions. Malarial therapy was given, the patient improved and went away. The lesions then returned and this time the patient had a positive Wassermann reaction instead of the negative reaction which he previously had. When his Wassermann reaction became positive Dr. Dennie gave him mercury, arsenic and iodides, with rapid disappearance of the lesions. There are so many instances of patients with a negative Wassermann reaction who have syphilis that as a profession we often discredit the negative Wassermann test; and yet in these cases called Wassermann-fast we practically persecute patients with intensive treatment to secure a negative reaction which we do not believe in after we get. I heard Dr. Keidel once say on a visit to Richmond that he did not like to see his patients become Wassermann-negative too quickly, because it indicated to him some lack of ballast in the immunological process. We seem to be afraid to bow down with John Kolmer to the Wassermann test as evidence of the condition of our patients. I cannot help believ-

ing that a positive Wassermann is good news and not bad news, as Cecil and other internists consider it. The patient's resistance has a large bearing on the success of the therapy which we adopt.

Dr. Hugh J. Morgan, Nashville, Tenn.—Two years ago, at the meeting of the Association for American Physicians, Drs. Cunningham, Seale Harris, Jr., Thompkins and I presented some work which tended to prove that the microphage that Dr. Dennie referred to in his paper was the dominant and characteristic cell in the lesions of experimental syphilis in the rabbit. Its presence was so constant and so striking that we felt that if we could employ some means of stimulating it we might modify the course of the disease. We used trypan blue, which does stimulate the production of these cells, and found that we could favorably modify the course of syphilitic infection in the rabbit. We felt that in doing this we were employing a means of combating the infection through a mechanism native to the animal. Dr. Dennie's ideas regarding clinical syphilis tend to fall in line with this experimental work.

Dr. Paul F. Stookey, Kansas City, Mo.—I have had an opportunity to see many of Dr. Dennie's patients who have been treated with malaria, many more than he has shown you today. Some of his therapeutic accomplishments in malignant syphilis have been startling. I think it was Kyrle who recommended that malarial therapy be used in all cases of syphilis. This is a radical statement, but in those cases that do not respond to the ordinary treatment, and particularly in those cases that are arsenic-resistant, malaria is a valuable adjunct.

Dr. David W. Goldstein, Fort Smith, Ark.—Before inoculation with malaria in such cases, I believe that other and safer methods, such as foreign proteid injections, should be considered.

Dr. Dudley C. Smith, University, Va.—It should be mentioned, to have the discussion complete, that the remedies usually employed in syphilis (arsphenamine, mercury and bismuth) all have more than treponemicidal action. The *Treponema pallidum* will live in fairly good concentrations of these chemicals. These remedies have "resistance-building" properties.

There are certain clinical and pathological similarities between syphilis, tuberculosis and rheumatic fever. The only methods of treating the latter two are by long periods of complete rest with an abundant well-balanced diet. I sometimes wonder if it would not be valuable to emphasize these same factors more than we do in syphilo-therapy.

Dr. Dennie (closing).—I limited my talk to the action of one thing. It is not a complete paper at all. There are many other phases of treatment that are valuable and that could be discussed. I have used a great many typhoid injections and while the reaction is somewhat of the same nature as that due to the malarial parasite, it does not compare in any way with malarial therapy. In the interstitial cases it has some reaction, but it was several months before I obtained apparent results. In the lesions of the palms and soles I obtained some benefit from typhoid, but nothing like that secured by the use of the malarial parasite.

I am not advocating the use of malarial therapy in all cases of syphilis, but am trying to show that it is possible by some means to raise the immunity of the individual to his disease, and that malarial therapy is one means by which we may do this. We hope to find something less harmful and just as efficient in raising the immunity to that disease.

RUPTURE OF THE KIDNEY*

By EARL FLOYD, M.D.,
and
J. L. PITTMAN, M.D.,
Atlanta, Ga.

Our purpose in this presentation is to review the literature concerning rupture of the kidney and to report eight cases, emphasizing the end results as shown by study of function and pyelograms.

Emergency surgery is becoming one of our greatest fields, and injuries to the kidneys are proportionately on the increase. If such cases are to be interpreted correctly and promptly, all emergency hospitals should have on their staffs a urological surgeon.

It is said that Galen was the first to describe a case of kidney rupture in 1561, and Dr. Rowden the first to perform a neophrectomy in 1883 for a similar condition. Many cases have been reported since that time.

In the majority of cases the rupture is due to direct trauma, and Kusters'[1] hypothesis as to the manner in which it is brought about is presumably correct, that,

> "The hydraulic pressure, acting through the full vessels and the pelvis of the kidney, causes the organ to burst along the lines radiating from the hilum toward the point of maximum impact against the ribs, the opposing resistance being supplied by the vertebral column."

Six of our cases were due to direct trauma, and in one of these there was evidence of preexisting disease. Similar cases due to direct trauma have recently been reported by Delzell and Harrah,[2] Wesson,[3] Beach,[4] and others.

Indirect injury, such as a fall upon the feet or buttocks, may cause rupture of the kidney according to Jefferson.[5] Muscular action alone may rupture the kidney, as in a case reported by Fox.[6] Watson[7] reported a case of a boxer who received such an injury while delivering a blow.

Spontaneous rupture may also occur. Two of

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the eight cases that we are reporting ruptured spontaneously, and there was an antecedent pathological condition present in both. In the literature we were unable to find a single case of spontaneous rupture that did not have some pre-existing disease.

Many causes are listed as bringing about spontaneous rupture, such as tuberculosis, stones, infarcts, polycystic kidney disease, hydronephrosis, malignant tumors, and acute parenchymatous nephritis. In Amberger's[8] case arteriosclerotic changes and cystic degeneration were the only evidence to explain the rupture. Wade's[9] case, often quoted, was a bilateral rupture in an individual with acute parenchymatous nephritis. Tuffier[10] and Hartmann[11] reported cases due to malignant tumors. Several cases of spontaneous rupture of a hydronephrotic sac have been reported, one by Mathe,[12] and a similar case by Henline.[13] In the latter, the patient had had attacks of renal colic for a number of years. Judd's case, quoted by Thomas,[14] was unusual in that such attacks dated back fifteen years previous to the rupture.

In our traumatic cases, the pathological condition varied from mild lacerations to a complete rupture of the kidney. As a rule, it is the location, and not the extent, of the tear in the kidney that determines the seriousness of the condition. Infection was a complication in one patient, *Case 5* in this group, necessitating the removal of the kidney. The peritoneum was not torn in any of this series. When this occurs, it increases the gravity of the situation.

The process of repair of a ruptured kidney, according to Wesson,[15] is essentially the same as in any other parenchymatous organ. Connective tissue replaces the torn part and the function is decreased to a degree commensurate with the number of tubules destroyed.

In the cases where there is pre-existing disease in the kidney, as in spontaneous rupture, the kidney parenchyma ruptures more easily than in instances where the organ is not diseased. It is usually accompanied by hemorrhage and sometimes urine into the perirenal space, and frequently followed by an abscess.

The subjective symptoms in our cases were variable and sometimes misleading as to the severity of the injury. In two which were of a mild type of injury, there were hematuria and pain in the back. One patient was even in shock. In the severe injuries, there were shock, pain, tumor mass in the kidney region, and hematuria. These symptoms, however, were much less marked than would have been expected.

Hematuria seemed to be the most common sign. There are certain instances, though, such as the existence of clots in the ureter, severed ureter, or torn renal vessels, in which even hematuria may not be present.

A striking fact was that the severity of the lesion did not correspond with the severity of the pain. This point has been stressed by others. A complete rupture may cause only slight pain. As Papin and Ambard[16] have demonstrated, there are no sensory nerves in the kidney substance proper, and therefore the pain is not due to the injury of the kidney parenchyma. It is the increase of tension that causes the pain.

Rigidity over the affected side, in spite of the fact that there was very little pain, was a fairly constant sign.

Elevation in temperature was present on the second and third day in practically all of the cases. Absorption of the clots might account for it in a few of them.

EXAMINATION

Blood in the urine, in addition to pain and rigidity over the lumbar region in a patient recently hurt, points to kidney injury. Ureteral catheterization is perfectly justifiable in the event that an operation is to be done, for without a kidney on the opposite side, one might make the mistake of removing all the secreting kidney tissue that the patient has. Pyelography is defensible in spontaneous rupture and in those cases of the traumatic type where the diagnosis is doubtful. It is best, however, that one use a non-irritating solution like skiodan as a contrast medium.

Intravenous urography is of help in determining the presence of a kidney on the opposite side without cystoscopy.

Fractures and injuries to other organs sometimes occur at the same time as the injury to the kidney, as in Goinard's[17] case, and may mask it for a while. An exact diagnosis is then not always possible at first. Uncomplicated cases, though, as a rule, are not difficult to diagnose. It is the severity that cannot always be decided upon.

A differential diagnosis between kidney rupture and injuries to other portions of the genitourinary tract is sometimes necessary. Particularly is this true in small children. However, if one will systematize his urological examination,

the true situation can usually be determined. In *Case 3* it was necessary to differentiate kidney from bladder injury in a child.

The method we have used successfully in doubtful cases is as follows: a catheter is passed into the bladder. Should the catheter fail to drain urine from the bladder, after being introduced through an uninjured urethra, or drain only a small quantity of bloody urine, coupled with the symptoms of lower abdominal pain and muscular rigidity in a patient recently injured, one should suspect a rupture of the bladder. In case an injected solution fails to return, or only a small amount returns, one can be fairly certain of a ruptured bladder. If the bladder washings are clear, then the bleeding must be coming from the upper tract. A cystoscopic examination will remove any doubt.

TREATMENT

In the traumatic type, the mild cases recover with expectant treatment. Bed rest, an ice cap to the side, coagulants, and morphia constitute the usual form of treatment. *Cases* 3 *and* 7 were so treated. Such cases should be examined later and a pyelogram and function test done if the future welfare of their kidneys is to be considered. How many of these later on develop stones and infections we cannot say, for the statistics at the present time are of little value. Casper's case, quoted by Shapiro,[18] formed calculi after the rupture.

In severe injury a great deal of judgment in treatment is required. The symptoms, as stated before, may not be in proportion to the injury. Hematuria, which is one of the most common symptoms, may not respond to the usual simple measures and a transfusion may be necessary. This at least makes the patient a better operative risk.

All seem to agree that surgery is indicated in cases of profuse or persistent hemorrhage, extravasation, and infection. A nephrectomy should be done only upon those cases in which the bleeding is uncontrollable, the pedicle torn, or the pelvis or ureter is entirely severed along with the rupture, or if severe infection is present.

To be too radical and immediately remove the kidney merely because it has ruptured is not justifiable under modern conditions. On the other hand, it is hardly better to delay operation too long in cases of severe injury and allow complications to develop and bring about prolonged invalidism with possibly a subsequent nephrectomy.

In spontaneous rupture one should operate early as a rule. If the kidney is badly diseased, a nephrectomy should be done, provided the opposite kidney is capable of carrying on the work. As a prophylactic measure, it is a very good policy to do a nephrectomy in a case of complete destruction or a hydronephrotic sac, even though it is symptomless, for rupture may occur at some inopportune time from a very trivial injury.

REPORT OF CASES

Case 1.—O. M., a man, aged 25, was admitted to the Grady Hospital May 12, 1930, complaining of pain in the left lumbar region and over the crest of the ilium. He was injured while playing baseball, s'iding into a base, but was able to finish the game.

He was found to have some rigidity over the left kidney region, both in front and behind. The urine was loaded with red blood cells and the temperature was 99 to 101°. The blood in the urine was less on the second day, but became profuse on the third. He was transfused, but there did not seem to be any reduction in the bleeding.

Cystoscopic examination revealed spurts of blood coming from the left orifice. A catheter up the right ureter obtained normal urine.

He was operated upon and found to have a rupture of the upper pole which apparently extended into the superior ca'yx. The kidney was enlarged and there were dense adhesions around it which could not possibly have formed in the short time since the injury. (He

Fig. 1

Pyelogram showing deformity in superior calyx of left kidney. Picture taken six months after operation for rupture of the kidney.

stated later that he had had pain in that side on previous occasions.) The kidney was sutured and tubes left in for drainage.

The diagnosis was rupture of the upper pole of the left kidney. The kidney showed evidence of previous disease.

He was re-examined six months later. There was an occasional pus and several epithelial cells in the left kidney specimen; kidney function was practically normal, but the pyelogram showed a deformity in the superior calyx of the left kidney.

Case 2.—E. P., a boy, aged 10, was admitted to the Georgia Baptist Hospital during the night of May 1, 1929. He had fallen out of a tree and sustained an injury to the left side of his body on the previous day. The temperature was 99°, pulse 90, and respirations were 24. He complained of pain over the left kidney region. The urine was bloody. The x-ray showed a detachment of the head of the eleventh rib on the left aide. The hemoglobin was 70 per cent and the red blood count 3,520,000.

He was given a blood transfusion on the first day and another transfusion on the second. He continued to pass large quantities of blood and there was some bulging in the left flank. The pulse rate increased to 120 and there was marked pallor. He was operated upon 48 hours after entry. There were several blood clots in the perirenal space and a rent was felt in the upper pole of the kidney. There was considerable bleeding and no attempt was made to suture the kidney. It was packed with gauze and the wound closed. He left the hospital on the thirteenth day cured. This patient was re-examined two years later. The pyelogram showed the left kidney to be normal.

Fig. 2
Pyelogram showing the left kidney to be normal. Picture taken two years following operation on the kidney.

Case 3.—H. H., a boy, aged 9, was admitted to Grady Hospital May 8, 1930, having been in an automobile accident. He was in a state of shock and talking at random. There were bruises and lacerations over the entire body, more so over the left lumbar region. He complained of pain over the left kidney and the bladder. He voided several times, as much as one ounce at a time. The urine was dark and bloody. The temperature was 96°, pulse 130, and respirations were 18.

A catheter was passed into the bladder and drained a small amount of bloody urine. Twenty c. c. of boric acid solution were injected into the bladder. That amount returned and a little more. This specimen was only one-fifth the bloody consistency of the voided specimen. The second irrigation returned clear.

X-ray of the pelvis was negative for fracture. The right side of the abdomen was relaxed, but there was rigidity and tenderness over the left kidney.

A diagnosis was made of laceration of the left kidney. After the boy had been under observation eight days the bleeding stopped and he was dismissed well.

He was re-examined on May 26, 1931. There was 70 per cent output of dye in one hour and ten minutes after an intramuscular injection of 1 c. c. of phenolsulphonephthalein.

This case shows the value of a systematized manner of examining the urinary tract when in doubt.

Case 4.—F. S., a woman, 30 years of age, was admitted to the Grady Hospital on July 3, 1931. She had fallen down a hill, injuring her right side, and had been unconscious for about ten minutes. She passed some blood in the urine. There was tenderness and rigidity over the right kidney region. She complained of pain over the entire abdomen. The red blood cells were 3,145,000 and hemoglobin 65 per cent.

Ureteral catheterization was done, followed by a pyelogram on the right side. The x-ray showed an extravasation at the middle calyx of the right kidney. Expectant treatment was carried out for three days. The temperature was gradually rising and the rigidity of the right side remained. An operation was decided upon on the fourth day. She was found to have a

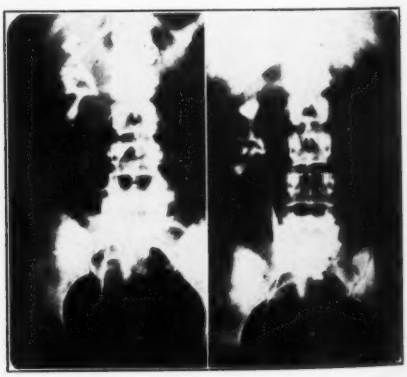

Fig. 3
The left pyelogram shows the extravasation of the iodide due to rupture in the mid-portion of the kidney. The right pyelogram shows the kidney three months following the operation.

sub-capsular tear on the posterior surface at the mid-portion of the kidney. Several clots were removed and the kidney was packed with gauze.

She was re-examined three months later. The right kidney specimen was negative, kidney function was normal, and the pyelogram showed a good draining kidney.

Case 5.—B. G., a boy, aged 13, was admitted to the Grady Hospital on August 29, 1928. He had been knocked off a bicycle by an automobile. The chief symptoms on entry were shock, pain in the left kidney region, both behind and in front, and tenderness and distention throughout the entire abdomen. There was crepitation of the last two ribs on the left side. The urine was bloody. Temperature was 99°, pulse 120, and respirations were 20.

On the second day the temperature was 102° and the pulse 110. There was some bulging and pain over the left kidney. The urine continued bloody. On the third day the temperature was 103° and the pulse 110. The urine contained some blood and the rigidity over the left kidney region remained. There was nausea and vomiting. The white cell count was 21,100, red blood count 3,312,000, and the hemoglobin 60 per cent.

Cystoscopic examination was done. The right catheter did not drain well; the left catheter specimen showed normal urine.

An operation was decided upon because of hemorrhage and infection. At operation there was found a complete rupture and evidence of infection. The kidney was removed.

The infection in this case had a great deal to do with the decision to remove the organ. The resu!t was good.

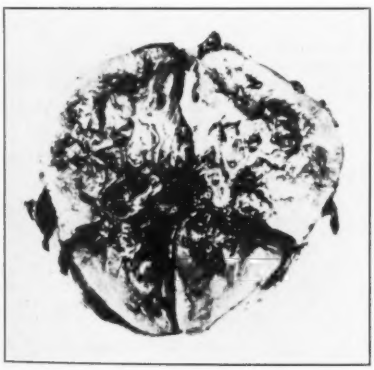

Fig. 4
Shows complete tear of the kidney.

Case 6.—J. R., a man, aged 61, was admitted to Grady Hospital on January 13, 1931. The chief complaint was a dull pain in the upper left quadrant of the abdomen. This pain had been present three weeks.

On examination a mass could be felt in the upper left side of the abdomen extending from beneath the costal margin across to the midline and down to the umbilicus. It could also be felt behind in the left lumbar region, or rather an indurated mass could be felt there. The mass was firm, but not nodular. There was an atrophy of both testicles. The prostate by rectum was of normal size and consistency. The urine showed a trace of albumin and a few pus and red blood cells. The patient stated that he had passed blood in the urine eight years previously. The red blood count was 3,790,000, hemoglobin 70 per cent, and white blood count 10,100. The temperature was 98 to 99°.

Ureteral catheterization was done. The right kidney specimen was normal with good function; the left had no function. No urine was obtained. The pyelogram showed extravasation of the iodide into the perirenal tissue.

Fig. 5
Pyelogram of left kidney showing extravasation of the iodide into the perirenal fascia.

Operation revealed a destroyed left kidney with extensive perinephritic abscess. There was a rupture at the lower pole. The patient died of sepsis eight days following operation.

The autopsy revealed a completely destroyed kidney, leaving only a cortical shell with three communications externally. There was a moderate amount of green pus about the kidney.

Case 7.—H. P., a boy, aged 14, was admitted to the Grady Hospital on November 18, 1929, complaining of pain in the left lumbar region and the passage of blood in the urine. He was injured while playing. A boy fell on his back.

On examination, there was some rigidity over the left kidney. The urine showed innumerable red blood cells. The x-ray was negative. A diagnosis was made of laceration of left kidney. He was dismissed eight days later as cured.

Re-examination in June, 1931, revealed normal urine and good kidney function. A uroselectan picture showed the kidneys normal.

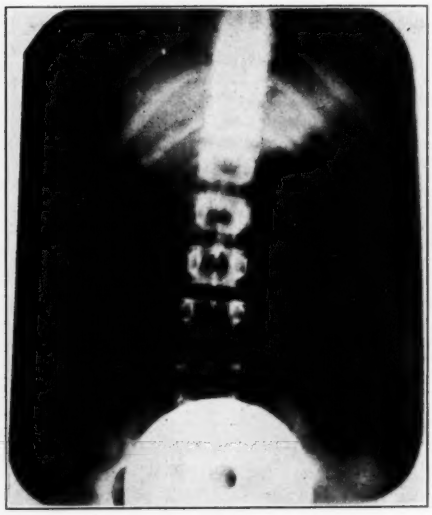

Fig. 6
Uroselectan picture shows the kidneys normal.

Case 8.—R. R., a man, aged 39, was admitted to the Georgia Baptist Hospital July 27, 1930. The chief complaint was pain in the right side of the abdomen. For the past four years some pain had been present, which had been severe for the past thirty days. Elevation in temperature had been present seven days.

Nine years before he had passed blood in the urine and had been treated for cystitis. He had not noticed blood since.

On examination there was marked rigidity over the right side with tenderness and bulging behind. The temperature was 101°. The urine showed an occasional red blood cell and pus cell. The right kidney function was impaired. The specimen showed a few pus cells. No red blood cells were recorded.

An x-ray was taken followed by a pyeloureterogram. The first picture showed a stone in the lower part of the kidney; the second, a deformity.

At operation he was found to have a rupture of the kidney at the site of the stone and a perinephritic abscess.

Our conclusion was that he had had this stone for at least four years and possibly longer. Pressure over a period of time produced a rupture at this point with extravasation of blood into the perirenal tissue. The clot became infected and an abscess formed.

Three months following operation the kidney function was practically normal; there were a few pus cells in the specimen and the pyelogram showed the kidney approaching normal.

SUMMARY

Eight cases of rupture of the kidney are herein reported. Six are of the traumatic variety and two of the non-traumatic or so-called spontaneous rupture.

Pyelograms were done on both cases of spontaneous rupture, but only on one of the traumatic variety before operation.

The end results of each case were determined, either functionally by means of kidney function tests and pyelograms, or pathologically by a nephrectomy or necropsy.

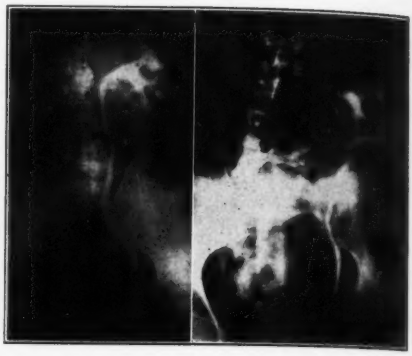

Fig. 7
The right pyelogram shows a deformity of the right kidney with a stone in the lower pole. The left pyelogram shows the kidney three months following operation.

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605 Doctors Building

DISCUSSION (*Abstract*)

Dr. N. F. Ockerblad, Kansas City, Mo.—Many ruptured kidneys are overlooked. As Dr. Floyd pointed out, many of them get well without surgical interference, but one does not always know the extent of the lesion from the symptoms. Several years ago I saw a nurse who had pus in her urine and a rather peculiar x-ray shadow. She had had a fall at the age of 8 years and injured her side. She was operated upon then by a well-known surgeon, who reported that she had a kidney tumor and would certainly die. Twelve years later, we got a peculiar opacity of the lower half of the kidney. There was permanent damage, but the patient had survived a very severe kidney rupture. So many of these cases do get well that we do not know the extent of the lesion which will recover spontaneously.

Dr. Monroe Wolf, New Orleans, La.—I have had a case of polycystic kidney with traumatic rupture of a cyst into the pelvis, which is of interest from a medicolegal standpoint. The patient had fallen while at work. A bilateral pyelogram showed typical bilateral polycystic kidneys with the cavity of the ruptured cyst partially obliterated.

This patient made an uneventful recovery under palliative treatment.

Dr. R. A. Hennessey, Memphis, Tenn.—Dr. Floyd has properly emphasized two important points in traumatic lesions of the kidney. The first concerns the necessity of painstaking study and determination of the extent of the injury. The second is the favoring of a conservative attitude in treatment, since it is known that the kidney is capable of great recuperation. I have had a case with extensive diffusion of the pyelographic medium into the perirenal tissues. There was spontaneous complete repair.

In another case of injury in a child of five, pyelography revealed a deformity suggesting a large solitary cyst in the midrenal area, with marked renal damage. Nephrectomy was done, and a large hemorrhagic cyst found, bisecting the kidney.

Dr. Robert F. Sharp, New Orleans, La.—We have pyelograms of a white laborer who received a severe blow in the right lumbar region eighteen days before being admitted to Charity Hospital. He was unconscious for a few minutes after the injury and remained in bed for one week, during the greater part of which time the urine was grossly bloody. By the end of the first week the urine had cleared up and he was able to be up and about and was fairly comfortable. Three days later, while stooping over, he developed a severe pain in the region of his injury and blood reappeared in his urine. Following this, he remained in bed for about one week and then went to Charity Hospital, where a pyelogram showed the right kidney to be ruptured with a great deal of the pyelographic media extravasated into the perirenal space. The patient was not severely toxic on admission to the hospital and ran a very slight febrile course during his stay there. The ruptured right kidney was removed.

This case was of interest to me because of the length of time that elapsed between the injury and the time of admission into the hospital, the slight systemic symptoms from a severe rupture of the kidney, and because the pyelogram showed marked extravasation of the pyelographic medium.

Dr. G. V. Brindley, Temple, Tex.—An apparently trivial injury may result in rupture of the kidney. Some years ago some boys were playing leap-frog and the boy who was leaping fell and his elbow hit the boy under him in the loin. He was brought to the hospital with a rather rapid, feeble pulse and a tender mass in the right loin. Voided urine was quite bloody. Upon exploration of the right loin, the right kidney was found to have an extensive laceration near the middle, practically dividing the kidney into two parts.

Dr. Floyd (closing).—It is possible that all of the cases we have reported of the traumatic type might have become seemingly well if we had not operated upon them, but I doubt that the end results would have been satisfactory. We must consider the future economic welfare of the patients.

TREATMENT OF COMPRESSION FRACTURES OF THE VERTEBRAE BY THE ROGERS' FRAME*

By JOSEPH I. MITCHELL, M.D., F.A.C.S.,
Memphis, Tenn.

Fractures of the spine are caused most commonly by indirect violence to the vertebral column through sudden forcible hyperflexion of the trunk. The body of the vertebra is involved more frequently than the neural arch and the fracture of the body is usually of the compression or impacted type, the body being compressed from above downward and becoming wedge-shaped with the base of the wedge posteriorly. The site of election is the mobile dorsolumbar segment of the spine extending from the eleventh dorsal to the second lumbar vertebra, the first lumbar being the one most often fractured; other common locations in order of frequency are the twelfth dorsal, the second lumbar, and the eleventh dorsal. Fractures of the other vertebrae are less common.

Diagnosis.—Compression fractures of the vertebrae may be overlooked at the time of the injury, simply because the immediate symptoms do not appear sufficiently severe to warrant a thorough examination. When the fracture is associated with paralysis of the trunk and extremities from hemorrhage, contusion, laceration or complete severance of the spinal cord, the diagnosis is obvious and as a rule appropriate treat-

*Read in Section on Bone and Joint Surgery, Southern Medical Association, Twenty-Fifth Annual Meeting, New Orleans, Louisiana, November 18-20, 1931.

ment, such as laminectomy for the relief of pressure, is instituted promptly. Many fractures of the vertebrae, however, are not complicated by spinal cord injury. In these unfortunate individuals the pathology may not be recognized, a diagnosis of contusion of the back or muscle strain is made and no treatment or ineffectual treatment is administered. When untreated, the patient is incapacitated for months and may be totally and permanently disabled. Since the majority of fractures of the spine occur in laboring men the economic loss to the patient, to his family and to his employer may be considerable. It is important that physicians realize that the physical findings alone in fractures of the spine are not always conclusive. Pain is usually present but may not be acute for several days. Stiffness of the back and soreness on pressure or movement are common and gradually increase in severity in untreated cases. On palpation a definite prominence of one of the spinous processes may be found and when the fracture involves the neural arch local ecchymosis may be apparent. A positive diagnosis can be made only by the roentgen ray. Both views of the entire spine should be made, as the lateral view often demonstrates fractures of the vertebral bodies more clearly than the antero-posterior view. Isolated fractures of vertebrae at different levels of the spine also occur more frequently than is commonly supposed and may be missed unless roentgenograms of the entire spine are secured.

Treatment.—The treatment of compression fractures of the vertebrae has received more attention in recent years since correct roentgen exposures have demonstrated the frequency of this injury and since the need for more accurate reduction has been experienced in compensation and other medico-legal cases. The results of treatment as in fractures of the other bones must be estimated by three factors, namely: anatomical reposition of fragments, correct alignment, and ultimate function. Correction of deformity of the crushed body is necessary to assure restoration of function to the spine. If uncorrected, the wedge-shaped vertebra produces a forward bending of the superencumbent vertebrae. The involuntary effort to maintain the erect attitude enforces, in turn, an exaggerated lumbar lordosis which results in muscular and ligamentous strain causing backache. The principle of treatment by hyperextension of the spine is well known but is difficult to carry out with ordinary hospital facilities. An extension frame designed to reduce the compression deformity of the vertebral body by gradual hyperextension was described by Rogers[1] in 1930. The apparatus is essentially a Bradford frame, excepting that chrome vanadium spring steel bands, broadside horizontal, are used instead of pipe or tubing for lateral bars. Canvas is stretched tightly across the frame as on the Bradford frame, and upon this the patient lies in the recumbent position. By means of a rachet attached to the bed, or by an overhead pully the lateral bands can be bent to render the frame concave or convex. The treatment is begun with the frame horizontal or slightly concave; continuous traction to the head or legs may be used in conjunction with the frame. As the frame is curved more and more convexly the spinal column is hyperextended, traction being exerted upon the vertebral body through the anterior spinal ligament and the inter-vertebral discs. The compression deformity is gradually corrected and the vertebra reassumes its normal contour and alignment.

The technic as originally described consisted of very gradual hyperextension over a period of several days, complete correction being secured in five or ten days. When the maximum correction has been obtained, as demonstrated by the roentgenogram, the patient is placed on a curved Bradford frame or a plaster of Paris cast is applied to maintain the corrected position for eight weeks. A spinal brace is applied before the patient is allowed to be ambulant, and this is worn for three to six months, depending upon the severity of symptoms. This procedure has been employed in our series of cases, and it is upon this technic that this report is based. More recently Rogers[2] has modified his technic so that correction is secured much more rapidly. The present plan is as follows: on admission to the hospital, the patient is placed on the frame and a preliminary morphin-scopolamin medication given, not enough to produce sound sleep but sufficient to relieve discomfort. During the course of the next half hour the spine is gradually hyperextended, a close check being kept on the reflexes during the hyperextension. As soon as the maximum correction is secured a snugly fitting cast is applied to maintain the position.

The method of gradual hyperextension is especially applicable to cases of fracture of the lower dorsal and lumbar vertebrae without paralysis. It has been used in one case with neurological symptoms in whom the Quickenstedt test was negative. When motor and sensory paralysis are present and the Quickenstedt test is positive indicating complete obstruction of the spinal canal, a laminectomy should be performed. The ap-

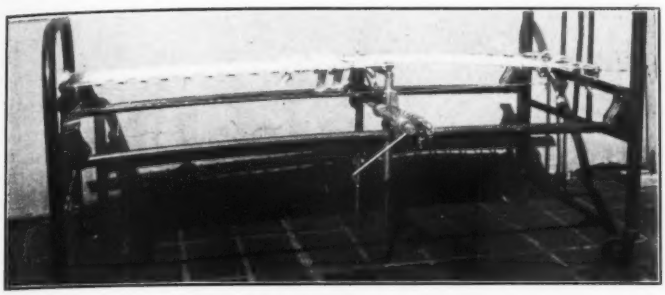

Fig. 1
Rogers' frame attached to bed. The frame is shown in the horizontal position with the rachet by which the central portion may be elevated.

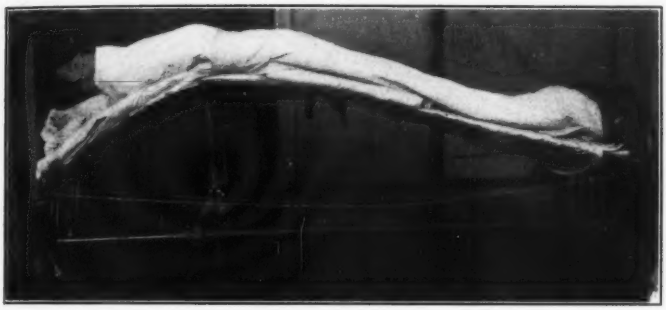

Fig. 2
The position of the patient when the frame has been raised to almost the limit of hyperextension.

paratus may be employed after laminectomy in favorable cases when the spinal cord is found not to be extensively traumatized so that a functional recovery is anticipated.

CASE REPORTS

Case 1.—E. H., a girl, aged 17 years, was admitted to the hospital May 21, 1930. One month previously, her back had been injured in an automobile accident. A diagnosis of fracture of the spine had been made by her attending physician, but no treatment administered other than rest in bed. The extensor muscles of the left foot were paralyzed and there was partial anesthesia of the left foot and leg below the knee. No deformity was apparent, but the lower back was tender on pressure and painful on motion. The patient was unable to sit erect or stand. The roentgenogram showed a compression fracture of the first lumbar vertebra with wedging of the body and forward dislocation of the twelfth dorsal on the first lumbar. There was also a lateral curvature of the spine convex to the left. The spine was hyperextended gradually on the Rogers' frame and on June 9 a cast was applied. Subsequent roentgenograms demonstrated correction of the deformity with excellent alignment. The cast was worn six weeks and a spinal brace for six months. The back is now normal in contour, and there has been no recurrence of pain or rigidity. The paralysis of the left foot persisted and a stabilizing operation was performed for this condition in June, 1931.

Case 2.—J. G., a farmer, aged 24 years, was admitted to the hospital May 28, 1930. He had been injured on the previous day by being thrown from a mule and landing on his back and shoulders. On examination, a slight kyphos was observed in the dorsal region with muscle spasm, tenderness, and rigidity of the spine. There was no paralysis. The roentgen ray revealed a compression fracture of the twelfth dorsal vertebra with wedging of the body. After extension of the spine on the frame for four weeks a cast was applied. This was worn for four weeks and followed by a spinal brace.

Fig. 3
Roentgenogram of Case 2 showing fracture of twelfth dorsal vertebra.

Fig. 4
Same as Fig. 3 after correction.

Fig. 5
Roentgenogram of Case 3 showing fracture dislocation of first lumbar vertebra.

Fig. 6
Same as Fig. 5 after correction.

Subsequent roentgenograms demonstrated that the normal contour of the twelfth dorsal vertebra had been almost completely restored. When last seen October 14, 1930, five months after the injury, the external appearance of the back was normal and all symptoms had subsided.

Case 3.—W. N. H., a farmer, aged 23 years, was brought to the hospital July 5, 1930. His back had been injured that afternoon when he drove a wagon load of hay into the barn and was caught under the door frame. The examination disclosed an angular kyphos at the dorsolumbar junction with tenderness, muscle spasm and pain on motion. There was no paralysis. The roentgenogram showed a compression fracture of the first lumbar vertebra with forward displacement of the body of the first lumbar on the second lumbar. The transverse processes of the first lumbar vertebra were also fractured. The routine treatment was administered, the cast being applied after three weeks. Roentgenograms then demonstrated a normal relation between the twelfth dorsal and first lumbar vertebra. A spinal brace was fitted September 2. The convalescence was uneventful, complete relief of symptoms being secured.

Case 4.—J. J. A., a mechanic, aged 29 years, was admitted to the hospital September 18, 1930, one hour after his injury. While working under an automobile which was suspended by chains, one of the chains slipped, letting the car fall on him, forcing his spine into the acutely flexed position. The examination showed a contusion over the left capula and a mild kyphos at the dorsolumbar region. Pain on movement was severe, but there was no paralysis. The roentgen examination demonstrated a compression fracture of the twelfth dorsal vertebra. The spine was hyperextended on the Rogers' frame and three weeks later a cast was applied. Roentgenograms through the cast showed almost complete restoration of normal contour to the crushed vertebra. A spinal brace was applied November 18 and worn until March, 1931. The symptoms were entirely re'ieved and function of the back is normal.

Case 5.—A. T. S., a farmer, aged 44 years, was injured November 3, 1930, when a bale of cotton which he was unloading from a wagon fell on him. Motor and sensory paralysis was complete below the level of the umbilicus, including loss of bladder and rectal sphincters. When admitted, the patient was in a state of moderate shock. There was a hematoma about the dorsolumbar area and a kyphos at that level. The roentgenograms revealed a comminuted fracture of the body and laminae of the

Fig. 7
Roentgenogram of Case 4 showing fracture of the twelfth dorsal vertebra.

Fig. 8
Same as Fig. 7 after correction.

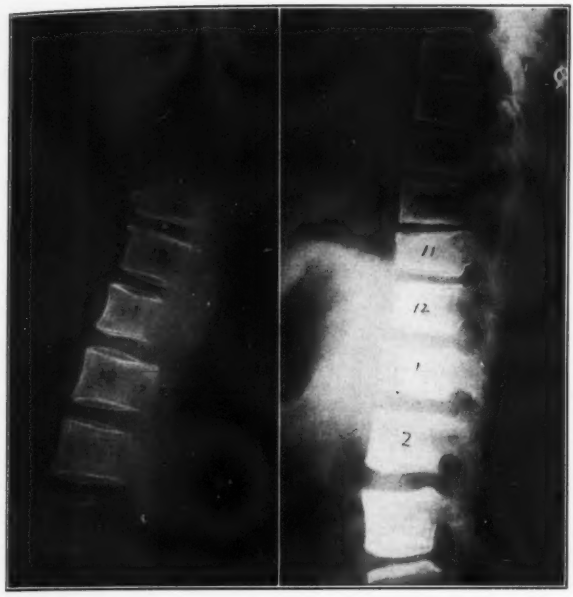

Fig. 9
Roentgenogram of Case 5 showing fracture of the eleventh dorsal vertebra.

Fig. 10
Same as Fig. 9 after correction.

eleventh dorsal vertebra; there was slight lateral and backward displacement of the tenth on the eleventh vertebra. A spinal puncture revealed blood-stained fluid and the Quickenstedt test was positive. A laminectomy was performed by Dr. R. E. Semmes. The spinal cord was found contused but not lacerated. The bony pressure was relieved and the patient returned to bed on a Bradford frame. Two weeks later when the operative wound had healed he was transferred to the Rogers frame and the spine gradually hyperextended. A cast was applied December 8, and a spinal brace January 13, 1931. Subsequent roentgenograms demonstrated practically normal contour of the vertebral bodies. The paralysis has gradually improved; the patient has regained control of the bladder and rectum and walks with assistance. At the present time there are no symptoms referable to the back.

Case 6.—R. D., a waiter, aged 21 years, came for examination November 20, 1930, because of pain in the back following an automobile accident seven weeks previously. For two weeks after the accident he had remained in bed most of the time but had received no definite treatment. The examination showed a spinal curvature which the patient stated had been present most of his life. There was also a kyphos in the upper lumbar area which had been noticed only after the injury. Movement of the spine was painful and limited in all directions. The roentgenograms revealed a compression fracture of the third lumbar vertebra and fracture of both transverse processes. The second lumbar vertebra was displaced forward on the third; there was a spina bifida of the fifth lumbar vertebra; and a right dorsal, left lumbar scoliosis. Correction of the deformity was attempted by gradual hyperextension, the patient remaining on the frame for five weeks. A cast was then applied and on March 10, 1931, a spinal brace was fitted. Only slight improvement in bony contour was secured probably because of the length of time elapsed before treatment was instituted. The symptoms have been greatly relieved, although when last seen the patient stated that his back was still weak and that he tired easily.

Case 7.—E. S. D., an office worker, aged 36 years, was brought to the Clinic December 2, 1930, by his physician. Five days before, while being initiated into a fraternal organization, the patient had been dropped fifteen feet into a tank of water. His hands and feet had been tied together so his back was acutely flexed. Immediate severe pain had been experienced in the back and referred to the abdomen, but he had walked with assistance to his home several blocks away. The pain increased in severity and the following morning he was unable to get out of bed. An osteopath was called, but as the pain still increased after several manipulations, the physician was finally consulted four days after the injury. The physician made the diagnosis of fracture of the first lumbar vertebra which was confirmed by the roentgen ray. The routine treatment was instituted, the patient remaining on the frame for three weeks and wearing a plaster cast for four weeks. A spinal brace was then fitted, which he wore for six months. The result both roentgenologically and functionally is excellent.

Case 8.—J. L. L., a farmer, aged 32 years, was examined January 7, 1931. He had injured his back seven weeks previously by falling from a tree, but had received no treatment other than rest in bed. The examination showed rigidity of the spine with loss of the lumbar lordosis and a kyphos at the dorsolumbar region. Pain and tenderness were present over the second lumbar vertebra. The roentgenograms demonstrated compression fracture of the second lumbar vertebra with wedging of the body. The spine was hyperextended for four weeks on the Rogers' frame and the extended position maintained for eight weeks longer in a cast. Only moderate correction of the deformity was secured but the symptoms have been completely relieved.

Case 9.—F. M., a woman, aged 28 years, was examined May 21, 1931. One month previously she had sustained an injury to the back in an automobile accident. There had been little discomfort at the time of the accident, but later she had noticed pain and a feeling of tightness in the back. On examination there was no deformity of the spine. Motion was somewhat limited and there was tenderness on palpation over the lumbar muscles on the right side. The roentgenograms showed a fracture of the first lumbar vertebra with slight compression of the superior margin of the body. An interesting incidental finding was a tumor in the pelvic cavity which contained numerous teeth. This was removed later and proved to be a teratoma of the right ovary. Treatment of the fractured vertebra consisted of hyperextension of the spine for eighteen days. On June 11, a cast was applied, maintaining the corrected position, and roentgenograms at that time demonstrated complete restoration of bony contour. In August the cast was removed

and a spinal brace fitted. The symptoms have been entirely relieved, although it is too early to make a definite statement as to the final result.

Case 10.—C. E., a woman, aged 46 years, was admitted to the hospital June 27, 1931. Ten days previously she had fallen backward off a porch, a distance of five feet and struck the ground on her back. There was immediately severe pain in the back which was referred to the abdomen and was associated with nausea and vomiting. When she was admitted to the hospital the abdomen was so distended with gas that the intern made a diagnosis of intestinal obstruction. Fortunately, roentgenograms of the spine were secured before she was subjected to laparotomy, and they showed compression fractures of the eleventh and twelfth dorsal vertebrae. There was very little lateral or anteroposterior displacement. The spine was gradually hyperextended, and on July 22 a cast was applied. Roentgenograms through the cast showed improvement in contour of the spine, although the vertebrae have not been restored to their normal shape. It is possible that the reason the deformity of the vertebrae has not been corrected in this case is that, due to the compression of the two adjacent vertebrae, the integrity of the intervertebral disc has been impaired. The first cast was removed September 15, and a simple body cast applied which she is still wearing. The symptoms have been entirely relieved.

Case 11.—E. R. A., a woman, aged 26 years, was first seen July 30, 1931. Her spine had been injured July 22 in an automobile accident. The patient experienced severe pain in the lower back but was able to walk. After a few hours she found that she could not flex the spine because the pain was so greatly exaggerated. The examination showed tenderness over the entire lumbar area. The spine was held rigid by muscle spasm. There was no deformity and no paralysis. The roentgenograms showed a fracture of the first lumbar vertebra with wedging of the body. Extension of the spine was accomplished on the Rogers' frame. A cast was then applied and worn for six weeks, followed by a spinal brace. Roentgenograms show correction of the deformity and the symptoms are relieved.

Case 12.—Mrs. F. S. F., a woman, aged 21 years, was injured in an automobile accident September 18, 1931. She was admitted to the hospital the following day. The examination showed a swollen tender mass over the lower lumbar region in the mid line. There was motor paralysis of both legs below the knees, loss of sphincteric control, a saddle area of anesthesia over the buttocks extending down the inner side of the thighs and partial loss of sensation over the feet and ankles. The roentgenograms showed a fracture of the fourth lumbar vertebra with comminution and compression of the body. The spinous process of the third lumbar vertebra was fractured and the third and fourth vertebrae were displaced laterally on the fifth. A spinal puncture was performed and clear cerebrospinal fluid obtained. The Quickenstedt test indicated only partial blockage of the spinal canal, and after consultation with a neurological surgeon it was decided that laminectomy was not necessary. The spine was hyperextended on the Rogers' frame and subsequent roentgenograms demonstrated that the contour of the body of the vertebra had been restored. Sensation and motor power are gradually returning, but it is too early to determine the degree of functional recovery.

Case 13.—J. P., a young man, 20 years of age, was admitted to the hospital October 3, 1931. He had been injured twelve hours previously when an automobile backed over him, forcing his spine into the acutely flexed position. His injury consisted of a fracture of the base of the skull and a compression fracture of the body of the first lumbar vertebra. On admission there was paresthesia below the knees on both legs and slight muscular weakness of both feet. The Quickenstedt test was positive, indicating a complete obstruction of the spinal canal, and after three hours a definite increase in the neurological symptoms was evident. Laminectomy was performed by Dr. R. E. Semmes. The spinal cord was found compressed but not apparently damaged. As soon as the wound healed the patient was placed on a Rogers' frame and the spine hyperextended. The paralysis cleared up immediately and subsequent roentgenograms showed excellent correction of the vertebral body. The patient is still wearing a plaster cast but the prognosis for complete recovery is good.

Fig. 11
Roentgenogram of Case 13 showing fracture of first lumbar vertebra.

Fig. 12
Same as Fig. 11 after correction.

SUMMARY

During the past year and one-half, 13 cases of fracture of the spine have been treated at the Willis C. Campbell Clinic, using the Rogers' extension frame. The results in these cases have

been so uniformly satisfactory both radiologically and functionally and are so superior to the results obtained by treatment without strong hyperextension of the spine that it is believed that the method warrants more general recognition and wider usage. Eight of the 13 patients were men and 5 were women. The youngest patient was seventeen and the oldest forty-six years of age. The location of the injury in 11 of the cases was at the dorsolumbar area. The first lumbar vertebra was involved in 5 cases, the twelfth dorsal in 4 cases, the eleventh dorsal in 2 cases, and the second, third, and fourth lumbar vertebra in one case each. In one instance (*Case 10*) there was compression of two adjacent vertebrae, the eleventh and twelfth dorsal.

Associated spinal cord injury was present in 4 of the cases, in 2 of which laminectomy was performed and the patient later placed on the hyperextension frame. One of the paralyzed patients was not seen until one month after the injury and in another case the spinal canal was not blocked, as shown by a negative Quickenstedt test. Laminectomy was not thought to be indicated in either of these two cases. The functional result is, of course, materially affected by the complicating neurological symptoms and the prospect of the patient's ultimately resuming his former occupation is proportionately decreased. Of the 9 non-paralyzed cases the clinical results are excellent in every instance. In two of the paralyzed patients (*Case 1 and Case 5*) sufficient time has elapsed to determine the final result. Both have a permanent residual paralysis, but there are no symptoms referable to the fractured vertebrae. The remaining two paralyzed patients (*Case 12 and Case 13*) were injured recently but the paralysis in *Case 13* is clearing up rapidly.

The degree of correction of the compression deformity obtained by treatment varied, being influenced chiefly by the interval between the time of the injury and the institution of treatment. Eight of the patients were seen immediately or within the first week after the accident. Three were not seen until one month after the injury and in two cases two months had elapsed. In the delayed cases an attempt was made to correct the deformity by hyperextending the spine. The anatomical realignment, as might be expected, was not so satisfactory as in those cases treated immediately after the injury. Some degree of correction, however, was secured even after two months and the pain was relieved. Of the eight cases treated immediately, greatly improved alignment was secured in every instance, the normal contour of the vertebral body being almost completely restored.

CONCLUSIONS

Thirteen cases of compression fracture of the vertebral bodies have been treated by strong hyperextension of the spine on the Rogers' frame.

The roentgenograms have shown definite evidence of correction of the compression deformity in eight cases treated immediately after the injury. Partial correction was secured in the other five cases even after a duration of one to two months.

The method is especially applicable to fractures of the vertebrae uncomplicated by spinal cord injury. It may also be employed in cases with neurological symptoms when no bony obstruction exists or after the pressure has been relieved by laminectomy.

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DISCUSSION (*Abstract*)

Dr. Joseph B. Foster, Houston, Texas.—I was Dr. Rogers' intern in the Massachusetts General Hospital when the first apparatus that he devised was placed on one of the regulation hospital beds and used. This apparatus itself was an improvement upon the old Bradford frame method of treatment, but it required a reasonably good mechanic with wrenches, screw drivers, and pliers on rather constant duty to maintain the desired position.

Dr. Rogers then had the entire apparatus made in one unit and put on wheels with the ratchet that produces the hyperextension firmly fixed so that it would not wobble about. Other minor improvements were added until now we have the so-called Rogers or hyperextension bed which is proving to be one of the most valuable adjuncts ever devised in the treatment of compressed fractures of vertebrae. I do not remember how many cases were treated at the time I was an intern, but there was a goodly number, and so far as I can recall the results were all satisfactory.

In the early part of this type of treatment an anterior shell was made with the patient in the desired position on the bed and later a posterior shell was made which facilitated the handling and turning of the patient so that it would not be necessary for him to be on his back all the time. After the shell had served its purpose the patient was placed on a Goldthwaite frame in hyperextension and a body-jacket was applied to be worn a few weeks during which time he was allowed to be up and about. Later it seemed that the period of time spent in the shell was unnecessary; therefore, the patient was taken directly from the hyperextended position on the bed and the jacket applied.

I mention these steps thinking that you may be inter-

ested in the progressive history of this scheme for the treatment of compressed fractures of the vertebrae.

In reviewing some of the literature one finds that hyperextension is the classical method of treatment of compressed fractures of the vertebrae. Davis, of Erie, Pennsylvania, puts these patients on a table in the prone position and obtains hyperextension by drawing their heels high into the air. In this position he makes a posterior shell and later an anterior shell. The other writers, as mentioned above, all accomplish this measure by one means or another. However, it is usually accomplished gradually. I do not approve of forcible hyperextension under general anesthesia. This, to me, seems to be a dangerous procedure.

Recently there has been devised a Bradford frame which is adjustable so that hyperextension to any degree may be obtained. This, in itself, is an excellent device but would necessitate a frame for each and every patient; first, because all Bradford frames are not suitable for all patients; and, second, the angle of hyperextension would not come at the site of the lesion in all cases.

In a recent communication, Dr. Rogers informs me that he is now accomplishing his reduction in about thirty minutes under scopolamine and morphine, as mentioned by Dr. Mitchell. I have had no experience with this method, but can see that it is quite an improvement over the old one, as one is able to watch the reflexes and nervous manifestations while accomplishing a reduction.

I heartily endorse this method of treatment of compressed fractures of the vertebrae.

Dr. Fred G. Hodgson, Atlanta, Ga.—I have used this method with very satisfactory results.

There is one thing which I think we ought to emphasize and teach the public in regard to the transportation of these patients. Frequently they are picked up on the highway after an automobile accident and are sat up in an automobile and brought into the hospital sitting up. They should always be transported in the horizontal position, on a couple of planks, or a door, and a mattress. If they were turned on their face they would be very much more comfortable and less damage would be done during transportation.

Dr. J. S. Speed, Memphis, Tenn.—I was somewhat surprised and a little disappointed in Dr. Rogers' improvement on his original method. I cannot help but feel that the rapid reduction of any compressed fracture of the vertebrae, where the lumina are torn, is dangerous.

This method particularly appeals to me because it may be combined with a corrective method.

I hesitate to try the more rapid correction. The results that have been obtained by the gradual correction are all that could be desired from an anatomical standpoint. We have not seen any evidence of damage to the spinal cord during gradual correction, consequently I cannot see the advantage of increasing the rapidity of the correction except for the discomfort to the patient from a rather prolonged immobilization on the frame. In treating fractures of the spine in the past the injury to the spinal cord has been our chief concern. However, the opening out of the vertebrae and the restoration of its normal contour is an extremely important part of the treatment in these cases if we wish to prevent future disability.

I wish to say just a word again about the rapid return of these people to the horizontal position or to their work. I believe that it takes some little time for these bones to harden sufficiently to permit weight bearing on the vertebrae in the upright position. We have no type of brace or mechanical support which thoroughly or properly immobilizes the spine in these cases, and if the weight of the body is allowed to be thrown on the vertebrae at too early a period a recurrence of the compression is apt to occur. It is better for these cases to be kept in the recumbent position for a rather long period of time, certainly for at least three months.

Dr. J. Albert Key, St. Louis, Mo.—This beautiful series of cases tends to win me away from the method of Arthur Davis. I believe that he was the pioneer in the correction of the deformity. After Davis demonstrated that the deformity could be corrected by manipulation, Rogers devised his frame for the gradual correction, because he felt, as Dr. Speed does (and as many others do, but as I do not), that there is considerable danger in immediate correction.

Davis showed that the anterior ligament remains intact in compression fractures and is so strong that there is very little danger of increasing the damage to the spinal cord by manipulation in hyperextension. In cases with paralysis in which there is not a complete severance of the cord, immediate correction has a very definite place, and whether or not the method which Rogers has devised of putting the patients on this frame, giving them twilight sleep and pushing the frame up and obtaining the correction in a few hours will supplant this, I do not know.

I believe that laminectomies are a thing of the past, except in very rare cases, where it can be demonstrated by the x-ray that a lamina is pushed down on the cord. In other words, if the Quickenstedt test shows no blockage and the x-ray does not show a definitely displaced lamina, there is no excuse for laminectomy. When we hear of some one with a recent fracture of the spine who has had a laminectomy we now say, "Well, that finishes him."

I should like to ask how much pain these people have. In New York I saw a poor old lady strung up on one of these frames. She had been there for about two weeks and was having considerable pain.

Dr. H. Earle Conwell, Birmingham, Ala.—The importance of early diagnosis, early treatment with no weight bearing and with the patient in a recumbent position, cannot be over-emphasized in treating fractures of the spine.

The type of frame used by Dr. Mitchell shows that there are different roads that lead to Rome but that we may arrive at the same destination. I have been using the modified Herzmark convex Bradford frame in treating anterior compressed fractures of the spine, which I find is more adjustable and adaptable to the patient and the average hospital bed and also less expensive. By administration of a liberal dose of morphine and the early convexity of the frame with the patient on the frame the majority of cases of anterior compressed fractures of the spine can be reduced. In some cases we use traction to the head and pelvis for a period of several hours. I do not think that reduction of the anterior compressed fracture should be attempted under a general anesthetic except in selected cases and then only by expert hands.

The general condition of the patient should always be treated first. A thorough physical examination should

be carried out. The possibility that more than one vertebral fracture may be present, or other fractures in other parts of the body, as well as other complications, should always be thought of in fractures of the spine.

The importance of taking lateral x-rays, as mentioned by Dr. Mitchell, should not be forgotten. Too early weight bearing should not be carried out. I feel that the patient should be kept in a recumbent position for some time following a fractured spine.

Recently I had occasion to review 100 cases of fractures of the spinal vertebrae without cord injury, which I have observed at the Orthopaedic Clinic of the Employees' Hospital, and it was enlightening indeed to note that 40 per cent of these cases were anterior compressed fractures and that a large per cent of them were the results of automobile accidents. It behooves the general surgeon or the practising physician today to prepare himself better to treat these injuries, which are occurring more frequently than ever before.

Dr. Mitchell (closing).—I do not wish to take issue with Dr. Key or take credit away from Dr. Davis. However, in Cotton's "Textbook on Fractures and Dislocations," the statement is made that the manipulative treatment of the fractures of the spine is as old as surgery. I think that this is probably true. Many attempts have been made in former years to correct these deformities, but the method employed by Dr. Rogers is the most efficient and satisfactory one that has been devised. In my experience it has been very difficult to do it with the ordinary hospital facilities.

Concerning the degree of pain that these people suffer: most of them complain of abdominal distension from gas in the intestinal tract and I think that most of their discomfort is due to this, rather than to the hyperextension itself. When the maximum hyperextension is reached they also complain of tightness due to tension on the abdominal muscles. Otherwise there have been few complaints.

HEREDITARY ECTODERMAL DYSPLASIA OF THE ANHIDROTIC TYPE*

By RALPH BOWEN, M.D.,
Memphis, Tenn.

We wish to report the case of a five year old boy whose environmental adjustment resembles that of a turtle. He spends much of his time out of doors in a large tub of water, in which he submerges himself at intervals. He then resumes his play until his clothing needs further wetting. During the summer months his temperature is at all times between 101 and 105° Fahrenheit. He prefers to sleep on the floor or in the cellar. He has only one tooth. There is a persistent malodorous discharge from his nose.

*Read in Section on Pediatrics, Southern Medical Association, Twenty-Fifth Annual Meeting, New Orleans, Louisiana, November 18-20, 1931.

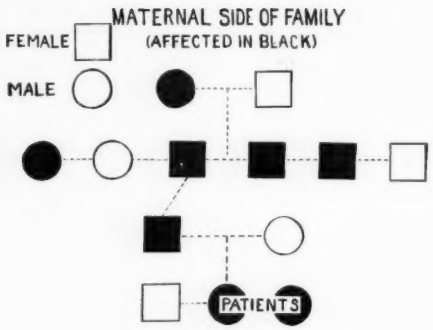
Weech,[4] in 1929, presented a comprehensive review of the syndrome and suggested that it be called "Hereditary Ectodermal Dysplasia of the Anhidrotic Type." This name seems most suitable, as the primary deficiencies are ectodermal in origin. On this basis, any case to be so classified must have the characteristics of the group, namely: a lack of sweat glands and pilosebaceous apparatus over most of the body, marked dental aplasia, depressed nasal bridge, atrophic rhinitis, smooth, dry skin, papular lesions on the face, and an intolerance to heat. These requisites are those proffered by MacKee and Andrews.[2]

Thurman,[3] in 1848, first described a case of this type. His patient, who lived to be 58 years of age, is the only one on whom a complete necropsy has been made. Gordon and Jamieson[1] recently reviewed the literature, in which they found but 21 cases between the years 1848 and 1929. They added one of their own, making the total 22. In 1930, Kerley[1] reported another case. No single observer has reported more than two cases. Although we are discussing only one here, we have found five others, to be described later, which will bring the number to 29. Since these five are members of three different families, we are led to suspect that the anomaly is more common than the paucity of cases in the literature would indicate. The six whom we have seen live within a radius of fifteen miles, but all deny any family relationship.

The present patient, R. C., a boy five years of age, was first seen a year ago. His parents are native Americans, living in the State of Mississippi. The child was born at full term and weighed eight and one-half pounds. During infancy he cried continuously, presumably from "colic," but probably from the discomfort of fever. He was fed artificially on various formulae. When two months old, an eczematous eruption appeared on his face and has never cleared. At the age of ten months he had his first and only tooth. Except for an attack of pertussis at two years, he has had no severe illness.

Since birth he has had a persistent, malodorous nasal discharge. Every summer he has had a daily rise of temperature, which makes him practically an invalid. His parents have observed that he is more comfortable on rainy days, and, as a consequence, they keep his clothing moistened day and night. When the weather is warm, a tub of water is placed in the yard, in which the child submerges himself from time to time as he plays. At night he sleeps in a damp cellar or on a wet mattress. During the winter he leads a more normal existence, as he is not uncomfortable and apparently has no fever. He has, however, a persistent generalized pruritis.

In early life his condition was attributed to an en-



GENEOLOGIC TREE OF FAMILY HAVING ECTODERMAL DEFECTS. THREE GENERATIONS.

Fig. 1.

docrine dysfunction, for which he was given dried thyroid gland. This increased his discomfort and induced further hyperpyrexia. For the past two years he has taken liberal quantities of cod liver oil.

Since he has only one tooth, he can take only soft foods or those which have been run through a sieve or food chopper. He enjoys sweets and milk. Hot foods apparently do not affect him. He has one normal bowel movement daily.

His voice has always been hoarse. His senses of smell and taste are considered normal. His mentality is good and he has a keen sense of humor.

The patient's genetic background is shown in *Fig. 1*. The union of the maternal grandfather, who had definite stigmata of the disorder, with an apparently normal woman produced six children. Four of these, one boy and three girls, had ectodermal dysplasia in varying degrees. One of the girls became the mother of this boy. The most persistent manifestation of the condition in this family has been dental aplasia. Only two, who are of the third generation, present features characteristic of the anhidrotic group.

The child's prematurely aged face was immediately striking. His expression suggested congenital syphilis. His scalp was covered by scant, fine, dry, lanugo hair; he had no eyebrows. An eczematous eruption covered his entire face. The forehead was normal; the supraorbital ridges were prominent, but the nasal bridge was depressed. The lower half of the face was incompletely developed on account of the dental aplasia. Both lips were thick; the upper was more prominent. His voice was hoarse and his speech slightly indistinct. The alveolar processes of both the maxilla and mandible were poorly developed.

His vision and audition were found to be normal. The septum was normal, but the mucous membranes of the nose were atrophic. The nasal discharge was peculiarly offensive. Roentgenological examination of the sinuses showed them to be cloudy. The one deciduous tooth was a tusk-like right upper central incisor. Two non-erupted teeth appeared in the roentgenogram; the permanent right upper central incisor and a lower molar. The latter were well formed. The membranes of the mouth and pharynx were thin and smooth. The tonsils were markedly enlarged. The thyroid gland was palpable. The chest was well formed except for a slight rachitic sternal depression. Both nipples were present. The lungs were negative to auscultation and percussion, as well as in the roentgenogram. Examination of the heart revealed no abnormality. The abdomen was normal in contour. The genital organs were normal in form and size. All reflexes were normal. The superficial veins were everywhere prominent. The skin of the palms of the hands and soles of the feet were cracked, fissured and caloused, resembling that of a person who does hard manual labor. Except for these areas and the eruptions on his face, the skin was white, dry, smooth and glossy. His nails were normal in size, shape, and consistency. Tactile and thermal sensations were normal. His height was 3 feet, 7-1/3 inches, his weight 37 pounds. The circumference of his head was 20-1/4 inches, chest 22 inches, and abdomen 20-5/8 inches.

The Wassermann and Kahn tests of the blood were both negative. The urine was normal. The blood showed hemoglobin 67 per cent, red cells 4,950,000, and white cells 9,600. The differential count showed polymorphonuclears 47, small lymphs 39, large lymphs 8, eosinophils 3, and basophils 0.

The roentgenological findings have been reported previously.

The history and physical findings were consistent with a diagnosis of hereditary ectodermal dysplasia. To confirm this, a portion of skin was taken from the axillary fold for histologic examination. The mi-

Fig. 2
Photomicrograph of section of skin removed from axilla. Sweat glands are absent. (Taken by Mr. J. Scianni.)

croscopic study, made by Dr. R. E. Ching,[5] revealed the following:

"Sections show a thin epithelium in which the cells on the basement membrane seem not so tall as is usual. Epithelium is seldom more than five or six cells in thickness and with very little keratinization. The derma contains no sweat glands or hair follic'es."

A photomicrograph is shown in *Fig. 2.*

These histologic findings, together with the clinical history and physical findings, place the case definitely in the group of hereditary ectodermal dysplasia.

Since the condition is not well known, these patients are subjected, as a rule, to a variety of treatments based on diagnoses ranging from endocrine dysfunction to congenital syphilis. The latter might easily be suspected because of the similarity of the facies. Endocrine therapy is contraindicated. As a matter of fact, since the underlying feature is an anatomic deficiency, medical treatment is to no purpose. One can only provide measures which will add to the comfort of the patient. If possible, they should live in a cold climate. Dental prosthesis is of value in preventing malformation of the jaws and aiding nutrition. Because of the familial

Fig. 3
Bodily configuration normal.

Fig. 4
Mouth opened to show upper incisor, right, the only tooth which has ever been present.

Fig. 5
Showing typical facies. Note thin, scanty hair, lack of eyebrows, depressed bridge of nose, scaly eruption on cheeks, poorly developed lower jaw. Hands show thickened and calloused epidermis.

Fig. 6
Roentgenogram showing only two unerupted permanent teeth.

nature of the anomaly, the patient and his parents should be warned concerning genetic transfer.

COMMENT

It is our impression that the condition is more common than the paucity of cases in the literature would indicate.

Practically all these cases are characterized by the features outlined by MacKee and Andrews, to which reference has been made.

There are no characteristic laboratory findings. Blood Wassermann tests, when made, invariably have been negative.

Reports of basal metabolism estimations have been unsatisfactory.

Cases reported in the literature show no definite familial trend. Our case, however, as shown in *Fig. 1*, suggests that the anomaly may be definitely hereditary.

SUMMARY

A patient with hereditary ectodermal dysplasia of the anhidrotic type is reported. The typical manifestations of this syndrome are presented. The total number of reported cases is brought to 29. It is important that these cases be recognized in order to prevent unnecessary and misdirected therapy. The futility of medical treatment is emphasized. Proper environment and the institution of dental prosthesis are indicated.

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The Polyclinic

DISCUSSION (*Abstract*)

Dr. Eugene Rosamond, Memphis, Tenn.—May I ask Dr. Bowen about the mentality of these cases, also about the danger of skin ulcers and the healing power of the skin?

Dr. Bowen (closing).—In all the cases I have observed the mentality was normal, and after injury wounds healed in a normal way.

At a later date I plan to report in detail five additional cases. In this connection I would like to mention two of these. The patients are brothers who live on a farm and work only during the early part of the day. While one is working, the other lies in a creek nearby in order to cool himself. In this relay fashion the day's work is completed.

As was mentioned in Weech's article, Guilford made a similar observation. His patient, also a farmer, had to have a boy throw water over him at intervals to prevent his fainting.

Dr. Jarret's report has already proved the syndrome to be not so rare as the literature would have us believe.

THE VALUE OF THE SCHILLING DIFFERENTIAL BLOOD COUNT IN PEDIATRICS*

By W. Ambrose McGee, M.D.,
Richmond, Va.

The importance of routine blood examination is far-reaching and there is no branch of medicine or surgery which is not frequently dependent upon it. Unfortunately clinical observations often fail to parallel blood findings. Reliance upon the present (Ehrlich) differential blood count offers no promise of relief from such confusion, but the new interpretation of white cells by Schilling[1] presents us with greater diagnostic and prognostic information.

In 1904, Arneth[2] called attention to immature blood cells in acute infections. His classification was so complicated that it has not been

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popular. Schilling's[1] revision of Arneth's classification with four simple groups opened up new possibilities for differential blood studies.

Schilling[3] recognizes three main divisions of white blood cells, namely: granulocytes, monocytes, and lymphocytes. An increase in granulocytes is noted in acute infections, in monocytes, in subacute infections and in lymphocytes in chronic infections. The changes in granulocytes, especially neutrophils, in acute infections, is the main factor in interpreting blood smears by Schilling's classification. He subdivides the neutrophilic granulocytes or "polys" into four groups: segmented or mature forms, stab (staff or band) or nearly mature cells, juvenile or immature forms and the myelocyte or youngest form of all. Both Arneth and Schilling speak of an increase in immature forms as a "shift to the left." The other white blood cells (basophils, eosinophils, lymphocytes and monocytes) are classified alike by Schilling and Ehrlich. Segmented "polys" consist of neutrophils whose nucleus is subdivided into two or more parts which are either distinct or connected by filaments. In stab cells, one sees a more or less continuous nucleus with heavy black pyknotic areas in it and a nucleus in the shape of an S, T, U, V, W or Y. Juveniles, also neutrophils, with a continuous nucleus normally shaped like a U or kidney or peanut; there are no dark pyknotic areas scattered through the nucleus, but there is a nucleolus in each terminal. In addition the nucleus of juveniles is paler, broader and usually ends in club-like extremities and in some instances the cytoplasm is pale bluish. Myelocytes have a single nucleus shaped like a ball or oval and their cytoplasm is distinctly blue with larger pink granules in it.

By arranging the leucocytes in a horizontal line it is possible frequently to predict the condition of the patient in question. Schilling refers to such an arrangement as a "hemogram."[4] Reading from left to right, the order of the leucocytes is basophils, eosinophils, myelocytes, juveniles, stabs, segments, lymphocytes and monocytes.

An increase in cells to the left of the segments indicates an increase in infection. When stabs alone are increased with a concomitant decrease in segments the shift is spoken of as a degenerative one. It represents an interruption in the developmental phase of the neutrophils by a toxic impression upon the bone marrow. With a stimulation of the regenerative process of the bone marrow by severe toxins, new cells are formed because of increased rate of manufacture. Such a change is referred to as a regenerative shift which is seen only in severe infection. Both degenerative and regenerative shifts may go on simultaneously. The use of the filament-nonfilament count as proposed by Mullen and Large,[5] while somewhat more simple than Schilling's classification, does not permit of such fine differentiation and requires the counting of 100 "polys."

A study of the other cells in the hemogram gives additional valuable information. An increase in basophils usually means a decrease in resistance.[6] The eosinophil is the most sensitive of all white cells and the first to disappear in acute infections.[6] In acute infections both lymphocytes and monocytes usually decrease in number and return when the struggle (infection) is over. A sudden rise in monocytes foretells the dawn of convalescence.[4] The monocytes reveal the defensive mechanism of the body.

After the monocytes have increased in number and the child continues to improve there is a reduction in the percentage of the shift to the left with an increase in mature "polys." This change is spoken of as a shift back to normal or a shift to the right. A concomitant high left shift with a high monocyte percentage indicates a good phase of defense with the battle (infection) still continuing. A very favorable sign after a shift to the right is the return of eosinophils and an increase in lymphocytes. This last change indicates recovery. In chronic infections with acute exacerbations of slight se-

Table 1

SUMMARY OF VALUE OF SCHILLING DIFFERENTIAL BLOOD COUNT IN PEDIATRICS

Average Variation of Hemogram of Well Older Infants and Children

Basophil, 0-1	Stab, 4-6
Eosinophil, 2-4	Segmented, 35-50
Myelocyte, 0	Lymphocyte, 30-55
Juvenile, 0-1	Monocyte, 3-6

Calculation of the Per Cent of the Shift to the Left

Division of immature neutrophils (stabs, juveniles and myelocytes) by total neutrophils (segments, stabs, juveniles and myelocytes).

Significance of Percentage Shift to the Left

Normal, 6 to 10 per cent
Slight infection, 11 to 30 per cent
Moderate infection, 31 to 50 per cent
Severe infection, 51 to 70 per cent
Danger of impending death, 71 per cent and over

Usual Blood Findings in Different Infections

Acute Infection.—Absence of eosinophils, increase in percentage shift to the left, low monocytes and lymphocytes.

Subacute Infection.—Absence of or very low eosinophils, lower shift to the left, increase in monocytes, slight increase in lymphocytes.

Convalescence.—Normal eosinophils, low or normal percentage shift to the left, normal monocytes, normal or increase in lymphocytes.

Chronic Infection.—Normal or slight decrease in eosinophils, continuation of shift to the left, normal or elevation of monocytes, normal or slight increase in lymphocytes.

verity, eosinophilia is usually noted along with a degenerative shift to the left.

The percentage of the shift to the left is determined by dividing the immature forms (stabs, juveniles and myelocytes) by the total number of neutrophils (segments, stabs, juveniles and myelocytes). The average shift for well older infants and children appears to lie

Table 2

VALUE OF THE SCHILLING DIFFERENTIAL BLOOD COUNT IN PEDIATRICS
HEMOGRAM IN ACUTE INFECTIONS

Age	Period of Illness	Basophils	Eosinophils	Myelocytes	Juveniles	Stab	Segments	Lymphocytes	Monocytes	Shift to Left Per Cent	Diagnosis	Remarks
V*		0-1	2-4	0	0-1	4-6	35-50	30-55	3-6	6-10		
2 years	2 days	0	0	2	19	25	21	25	8	68	Ac. tonsillitis	Ill
	3 days	0	0	0	12	14	34	25	15	43		
	5 days	0	0	0	0	19	41	35	5	31		
	7 days	0	2	0	0	8	24	64	2	25		Improved
3 months	1 day	0	0	0	5	23	12	54	6	70	Broncho pneumonia	Ill
	2 days	0	0	0	12	19	5	57	7	86		Very ill
	5 days	0	2	0	0	11	11	69	7	50		
	8 days	0	3	0	0	13	21	58	5	37		Better
	12 days	0	3	0	0	5	36	52	4	12		Well
5 years	14 days	1	3	0	1	12	22	53	8	37	Pertussis	W. B. C. 16,400
2 years	28 days	0	3	0	0	14	7	70	6	60	Pertussis and measles	
6 years	11 days	0	0	0	6	41	25	23	5	65	Measles	No rash
	13 days	0	4	0	3	10	14	58	11	48		Rash
	17 days	0	5	0	0	7	30	52	6	18		No rash
18 months	2 days	0	0	0	4	20	19	47	10	55	Pharyngitis	Acutely ill
	3 days	0	3	0	3	9	13	64	9	45	Roseola, Inf. Rash	Ill
	4 days	0	1	0	0	9	15	62	13	40		Better
	6 days	0	3	0	0	7	10	74	6	41		Practically well
18 months	2 days	0	0	0	0	1	2	93	4	33	German measles	Not sick
4 years	2 days	0	0	0	2	20	48	28	2	31	Scarlet fever	Onset
7 years	2 days	0	1	0	1	38	20	29	11	61	Chicken pox	Not ill
3 years	1 hour	0	0	0	8	22	16	47	7	65	Ac. Append.	W. B. C. 6,000
6 years	2 hours	0	3	0	2	19	42	28	6	33	Ac. Append.	Adenophathy
10 years	2 hours	0	1	0	9	21	50	17	2	37	Ac. Append.	Operation
	1 day	0	1	0	15	40	25	16	3	68		Improved
	2 days	0	1	0	2	36	36	18	7	51		Worse
	10 days	0	3	0	4	36	43	13	1	48	Pelv. Inflam.	
7 years	3 days	0	0	0	17	31	10	31	11	80	Intestinal "flu"	Ill
	5 days	0	4	0	1	22	17	40	16	57		Better
18 months	14 days	0	0	3	22	26	7	33	9	88	Ileo colitis	Moribund
	18 days	0	1	0	10	17	19	42	11	58		Better
10 years	14 days	0	0	0	0	28	26	40	6	52	Miliary tuberculosis	Sick
	18 days	0	3	0	0	23	29	30	5	44		Ill
	22 days	0	0	0	5	30	34	14	17	50		
	24 days	0	0	0	0	50	35	12	3	50		Moribund
2 years	6 hours	0	0	0	3	15	28	48	6	39	Laryngitis	Acute catar.
3 months	20 days	0	1	1	10	14	17	50	7	59	Mastoiditis	Surgical
18 months	12 days	0	6	0	0	13	47	28	6	21	Mastoiditis	Non-surgical
7 years	2 days	0	0	1	16	17	38	24	4	47	Poliomyelitis	Paralyzed
	3 days	0	0	0	0	12	60	23	5	17		
	4 days	0	0	0	0	7	54	33	6	11		Better
	5 days	0	2	0	0	5	52	36	5	9		

V*—Average normal variation of differential counts during infancy and childhood.

between 6 and 10 per cent. The severity of an acute infection is judged by the percentage shift to the left. Especially is this true when juveniles and myelocytes compose a large proportion of the left shift. In children one sees a slight infection with left shifts of 20 to 30 per cent; a severe infection when the shift is from 30 to 50 per cent and a very severe infectious process with a shift of 50 to 70 per cent. With left shifts higher than 70 per cent there is danger of impending death. In addition to the use of percentage shifts to the left as a means of judging the severity of infections, Gerard and Boerner[7] propose the use of the "nuclear index." The division of mature "polys" (segmented cells) by immature cells (stabs, juveniles and myelocytes) gives the nuclear index. In children the writer feels a nuclear index of 5 to 15 represents the average for well older infants and children; an index from 3 to 5 represents slight infection; of 1 to 3 a very severe infection and below 1 danger of impending death. A comparative study of the relative importance of left shift percentages, nuclear indices and filament-nonfilament counts shows the left shift percentage to be the most valuable method of estimating the severity of an infection.

Repeated hemograms are of more value than single determinations just as is true with physical examinations and temperature records. A hemogram taken at intervals (preferably 12 to 24 hours apart) frequently reveals improvement or relapse hours ahead of clinical observation. The Schilling differential study serves as a more sensitive indicator of changes in the body than either physical signs or fever.[8] Changes in total leucocyte counts[9] lag behind hemogram findings, as one frequently sees in suspected cases of appendicitis.

The Schilling differential count is of value in obstetrical practice[10] and in tuberculosis. After the diagnosis of tuberculosis is once established,[11] it is possible to foretell improvement or retrogression of the tuberculous process even days or weeks ahead of physical examination, fever, symptoms or x-ray findings. The shift to the left percentage and the lymphocyte-monocyte ratio[12] determine activity and healing in tuberculosis. If that ratio is 3 or over, Durel[13] feels healing is satisfactory and the prognosis, good.

The use of the Giemsa stain in studying leucocytes gives best results. Gradwohl informs us that the Giemsa stain as prepared in this country is unstable and that the best Giemsa stain is made by Hollhorn of Leipzig. Only grease-free glass slides should be used in making Schilling counts and the blood should be thinly smeared with a cover slip. Such a procedure prevents marginal accumulation of "polys" and permits a more detailed study of the leucocytes. The dried blood smear is fixed with chemically pure methyl alcohol for four minutes. After

Table 3

SCHILLING DIFFERENTIAL BLOOD COUNT
HEMOGRAM IN PERTUSSIS

Age	Leucocyte Count	Basophils	Eosinophils	Myelocytes	Juveniles	Stab	Segments	Lymphocytes	Monocytes	Shift to Left Per Cent	Nuclear Index	Results
V*	7,000-10,000	0-1	2-4	0	0-1	4-6	35-50	30-55	3-6	6-10	5-15	
9 years	21,000	0	1	0	0	12	32	51	4	27	2.5	Excellent
3½ years	30,200	0	0	0	0	4	31	60	5	11	7.0	Excellent
2 years	19,600	0	2	0	0	7	29	57	5	19	4.1	Excellent
5 years	16,400	1	3	0	1	12	22	53	8	37	1.7	Good
6 years	18,400	1	0	0	1	10	20	66	2	35	1.9	Good
15 months	46,000	0	1	0	1	10	13	71	4	45	1.1	Good
4 years	21,600	2	5	0	0	9	15	63	6	33	1.7	Fair
2½ years	14,200	0	4	0	0	10	15	65	6	40	1.5	Fair
3 years	17,200	0	1	0	0	9	20	65	5	34	2.2	Fair

V*—Average normal variation of white and differential counts during infancy and childhood.

that evaporates, freshly prepared Giemsa solution is added and allowed to remain for thirty minutes. The Giemsa solution is prepared by adding one drop of the Giemsa stain to one cubic centimeter of neutral distilled water. The aqueous nature of the Giemsa solution prevents rapid evaporation. After staining the smear the solution is flushed with neutral distilled water. A more rapid and equally efficient study of leucocytes can be made by a modification of the original Giemsa technic. The smear is first stained for one-half minute with Giemsa stain mixed with chemically pure methyl alcohol (one part Giemsa stain to two parts methyl alcohol), then the same quantity of neutral distilled water is added for two minutes, after which time the smear is flushed with neutral distilled water.

The value and significance of the Schilling differential blood count can best be understood by means of a few cases illustrating different points.

CONCLUSIONS

(1) The use of the Schilling differential blood count reveals much information relative to diagnosis, prognosis and treatment.

(2) It serves as a simple yet accurate index of changes taking place in the body in infections.

(3) Repeated hemograms are of more value than single determinations and they reduce the need of total leucocyte counts.

(4) Changes in granulocytes often reveal progress or relapse ahead of physical findings, symptoms, fever and total white cell counts.

(5) Information obtained from the Schilling counts should be used in collaboration with other clinical findings and symptoms, but an outstanding blood picture should not be ignored even in the absence of clinical symptoms.

(6) The present Ehrlich differential count is much less informative and should be replaced by the Schilling classification of leucocytes.

(7) Giemsa or modified Giemsa stain should gradually replace Wright's stain.

(8) The Schilling count is of more relative value than the filament-nonfilament count.

(9) It is of particular value among children, as it deals mainly with neutrophilic leucocytes rather than lymphocytes which predominate the blood picture in childhood.

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2618 Grove Avenue

DISCUSSION (*Abstract*)

Dr. I. A. Nelson, Tulsa, Okla.—The Schilling count has been a routine in the hospital in which I work now for three years. I have run the Schilling filament and Wright simultaneously in many kinds of cases. We have immature cells in all grades of development just as we have infants and children and adolescents. In teaching the method, we teach first the four granulocytes. The meaning of the monocyte and lymphocyte can be learned later. This is not a method exclusively for the laboratory man or pathologist, but is valuable for the pediatrician.

Dr. J. Shelton Horsley, Richmond, Va.—I have been very much interested in Dr. McGee's work in connection with the surgery of children. Someone has said that a specialist is one who knows more and more about less and less. The type of specialist who ignores the underlying biological laws may not be quite so desirable as one who takes a little broader view of the whole case.

I have called Dr. McGee in consultation on several cases and have found the Schilling test of value. One of the patients he has told you about: a little child who gave very slight symptoms of appendicitis. The shift to the left was quite marked, and on operation pus was found in the appendix. Twenty-four hours later, doubtless, the symptoms would have been more marked, but the early diagnosis and operation made possible by this test gave the child a better chance for recovery.

We look too much for one pathognomonic sign instead of considering all the signs and symptoms. If we pin our faith solely to the Schilling count for diagnosis and prognosis we shall be disappointed, though the Schilling test is an extremely important addition to our armamentarium for diagnosis. When we have a war we judge of its extent and severity by the number of volunteers called out, because the number of volunteers would indicate our estimate of the enemies we are to fight. So if nature calls out volunteers in great numbers it indicates a severe infection; if in smaller numbers, the infection is not severe. The young poly-

morphonuclear cells as classified by Schilling are the volunteers.

Dr. R. M. Pollitzer, Greenville, S. C.—Hematology has made tremendous strides in the last decade. Most of us were brought up to use Wright's stain, then taught to do a total leucocyte count, then a differential. Now we learn that these are not enough. If the Schilling test continues to prove to be as valuable as it seems to be in the hands of Dr. McGee and other workers, the next thing to ask ourselves is how practical it is and how easy of application.

I want to ask whether it is necessary to do the work with the Giemsa stain and whether the Giemsa stain keeps without deterioration.

Dr. McGee (closing).—The Schilling count can be done by any physician in the country or the city. All one needs is a microscope, a few glass slides and Giemsa stain.

It should be used in collaboration with other findings, but a high left shift should not be ignored even in the absence of physical findings. The total count, we know now, is worthless in many conditions. It is valuable in those in which we expect leucopenia, as malaria and tuberculosis.

With the modified Giemsa it is possible to prepare a stock solution which will last two weeks and which will require only three minutes for the total staining of the slide. With the use of the modified Giemsa it is possible to get much better and clearer results than by the use of the Wright stain.

DIET AND DIABETES*

By VIRGIL E. SIMPSON, A.B., M.D., F.A.C.P.,
Louisville, Ky.

There is as great variation in the food requirements of the healthy individual as there is in facial or temperamental characteristics. Individual, familial and racial factors are great fundamental influences determining both the kind and amount of food one needs; these, in turn, are further influenced by age, sex, surface area, muscular activity, climate, season.

But as one can recognize the myriads of human faces, or of personalities belonging to the genus *homo*, so may one adequately evaluate the varying agencies and conditions influencing the kind or quantity of food needed daily for a man. That a rather wide latitude of normal requirements, or a rather broad zone of adaptability to food resources exists is axiomatic, since in his primitive state man, tutored only by his special senses and instinctive guidance, attained development, growth and maintenance of health and activity paralleling reasonably closely those of our present day civilization.

Normal Diets.—From the study of the food supply of man under primitive conditions, coupled with the knowledge obtained by experimental data, medical service has formulated certain general statements concerning nutrition requirements. One of these general statements relates to caloric requirements of the body, so that one finds set down in the text-books of today the statement that the "average daily food requirements of the average adult" are:

1,500 calories when at rest
2,500 calories when taking light exercise
3,500 calories when at manual labor

The requirements for the average child are materially higher from a body surface viewpoint:

1,500 calories from 1 to 4 years
2,000 calories from 5 to 9 years
3,000 calories from 9 to 14 years

More accurately estimated, one may state these requirements in terms of heat units per kilogram of body weight. Such an estimate should be based on the approximate normal weight rather than the under or overweight which an individual patient may present. It may be stated that a diet furnishing 25 calories per kilogram may be reckoned as a basal diet, 30 calories per kilogram for moderate exercise and 40 calories for manual labor.

A yet more accurate method of estimation of food requirements consists in the use of some such table as that of Dubois and Dubois. By this table, 40 calories per square meter of body surface per hour with corrections for sex and age is considered adequate when the body is at rest and hence is termed a basal diet. With such a table a maintenance diet may be figured, understanding that by the term is meant a diet with a 24 hour caloric value adequate to meet requirements of a person taking his accustomed exercise.

Likewise, the protein requirement of the body has been determined and found to vary with age and activity. It is estimated that 0.75 grams of protein per kilo of body weight are needed to maintain nitrogen equilibrium for the average adult at rest, 1.0 grams for light exercise and 1.5 grams when at manual labor. This would comprise about 10 per cent of the daily food intake. Children, again, require a higher protein intake daily than adults from a body surface area viewpoint, from 2 to 3 grams per

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kilo of body weight being necessary between 10 and 14 years of age. About 15 per cent of the daily food allowance is thus represented by protein.

There is a fair degree of unanimity of opinion among laboratory workers and clinicians on body food needs as thus far stated, but disagreement, uncertainty, dogmatism and pragmatism keep the kitchen in an uproar from here on in. How much carbohydrate in terms of sugar does an average adult of average activity need? Every clinician answers at once and differently and bedlam reigns. The laboratory workers no longer speak with authority. Only mothers become dogmatic and pediatricians pragmatic and Junior is denied his coveted stick of candy.

What ratio should fat bear to the sugar content? The dermatologists disagree and gastroenterologists for once are uncertain. The diabetic specialists find in these two questions practically the only field in the management of diabetes where they may hope to have their names linked to a projected fatty-acid-glucose ratio for a brief season of popularity.

Shall the diabetic be admonished to still his hunger with firkins of butter, baskets of nuts, gallons of cream and cases of olive oil? Or shall he pay homage to the sugar bowl, the bread basket, the molasses jug and the preserves jar?

The ingestion, with relish and without insult to the digestive system, of large quantities of fat is an accomplishment of the Esquimo or the Norseman. To essay such a feat in New Orleans would be a self-written invitation to sojourn in a dietetic hospital. A fatty-acid-glucose ratio feasible in Minnesota would not be even sensible in Florida. And, as climate determines the fat intake, so will even season modify the relish for its use.

The ease with which heat units may be piled up and insulin dosage pulled down tempts the physician to figure high on fats. The hope that this is sensible farthers the thought that it is sound.

And, at the other extreme, the willingness of the diabetic to absorb insulin from under his skin that he may gluttonize in foods of high sugar content recruits votaries to the high and yet higher carbohydrate diet. If one could be sure that sugar, and yet more sugar oxidized by insulin, would actually increase the storage of glycogen in the liver the plan would, at least, become more debatable. But does storing glycogen really increase the oxidation of glucose in the blood? When diabetes is the diagnosis does it connote pancreatic deficiency or hepatic truancy? Does deficiency of the anterior lobe of the pituitary gland mean diabetes in any sense? Is the glycosuria of ventricular piqure what we understand to be diabetes? Does hepatic incompetency necessarily obtain in true diabetes? If a high fat diet does result in storage of fat in the liver, thus crowding out glycogen, that fact does not, *ipse facto*, mean that a high sugar intake automatically increases the native insulin activity. That expectation of an increased sugar oxidization is not rational is evidenced by the picture of the diabetic on an unweighed diet growing progressively worse as his insufficient oxidation of sugar whips up an appetite for more sugar and its ingestion results in greater hyperglycemia and greater pancreas tire. If a high fat diet abets storage of fat in the liver and excludes glycogen, then the answer is not an abnormal sugar intake, but a rational fat allowance.

Again, the advocates of a high sugar allowance admit that an increased insulin dosage is a corollary to that of increased sugar intake. For quick replacement of a normal weight and restoration of bread winning strength, one might readily concede the wisdom of high insulin unitage, but only as a temporary expedient. The diabetic rightly hopes to get rid of scales, of weighed diets and insulin. Is that a reasonable expectation? My clinical experience covering the period since 1923 justifies the belief that it is. An avoidance of extremes is a much prized desideratum in the diet of the diabetic, who is entitled to live as nearly normally as his disease will permit. His food should approach the normal as closely as one is able to determine the normal.

CALCULATION OF DIET

The nearest approach to a scientific basis for fixing the ratio that fat should bear to sugar is that furnished by the work of Shaffer. According to his data, fat can be oxidized completely if one part of sugar is oxidized for every one and one-half parts of fat. And in proportion to whatever degree of acidosis obtains must the ratio of fat to sugar be reduced. Guided by this data, I have been able to balance the diet of my diabetics satisfactorily. A table of diets covering all weights of patients, protein requirements, caloric needs and fatty-acid-glucose ratios

can be figured and utilized as a time saver at the office or bedside. Such a book of tables should be indexed so that the figures for any diet indicated could be turned to readily. *Table 1* is a sample page from such a book, from which a patient weighing 70 kilograms and estimated as requiring 1 gram of protein per kilo of body weight, a sugar tolerance of 160 grams and a caloric requirement of 1,978 heat units, can at once be given the figures furnishing these requirements.

Table 1

DIETS FOR A 70 KILOGRAM (154 LB.) PATIENT
PROTEIN 1.00 GM. PER KILO $\frac{F\ A}{G} = 1.00$

Diet No.	Carbohydrate	Protein	Fat	Total G.	Fatty Acid	F. A. G.	Calories	Calories Per Kilo.
638	7	70	20	50	50	1.00	488	7.0
639	16	70	31	60	60	1.00	623	8.9
640	25	70	42	70	70	1.00	758	10.8
641	34	70	53	80	80	1.00	893	12.8
642	43	70	64	90	90	1.00	1,028	14.7
643	52	70	75	100	100	1.00	1,163	16.2
644	61	70	86	110	110	1.00	1,298	18.5
645	70	70	97	120	120	1.00	1,433	20.5
646	79	70	108	130	130	1.00	1,568	22.4
647	88	70	119	140	140	1.00	1,703	24.3
648	97	70	130	150	150	1.00	1,838	26.3
649	105	70	142	160	160	1.00	1,978	28.3
650	114	70	153	170	170	1.00	2,113	30.2

The formula used in figuring such a table of diets may vary. Voit's standard, for example, for a man at manual labor, provides that 16 per cent of the total heat units of the day's food should be supplied by the protein, 18 per cent by fat and 66 per cent by carbohydrate. Thus if it were estimated that 3,000 heat units are to be furnished per day the ratio of carbohydrate, protein and fat would be 495 C.H., 120 P. and 60 F. According to more recent standards less carbohydrate and more fat are used. The United States Army ration (peace) furnishes 440 C.H., 110 P., 153 F., a caloric value of 3,577 and a fatty-acid-glucose ratio of 0.36.

A simple method of figuring such tables of diets is to decide the amount of protein to be given in grams, then determine the caloric value of the diet. The carbohydrate is found by subtracting from the total calories 10 times the protein and dividing the result by 20. The fat is determined by subtracting from the calories the sum of the carbohydrate and protein multiplied by 4 and divided by 9. This may be expressed by the formula:

$$\text{C.H.} = \frac{\text{Cal.} - 10\ \text{P.}}{20} \text{ and F.} = \frac{\text{Cal.} - 4\ (\text{C}+\text{P})}{9}$$

The tables I use were figured by Woodyatt's formula in 1923 by Dr. Fred. Speidel and furnish 13 diets in each table, the protein remaining the same, but the carbohydrate increasing 10 grams in each diet. The fatty-acid-glucose ratio of each table remains the same. To change the protein or the fatty-acid-glucose ratio another table must be selected.

Table 2 shows another page from such a book giving diets for a 70 kilo patient, each furnishing 1.5 grams of protein per kilo and a fatty-acid-glucose ratio of 1.50. The number of calories per kilo desired is located in the column headed "Calories per Kilo" and the proportion of carbohydrate, protein and fat to furnish that number of heat units and 1.50 grams of protein are found on the same line. The total glucose content, total fatty acids, and the total heat units are all set down. In using such a book of tables one merely determines the protein requirement and heat unit needs of his patient after the diagnostic study and then turns to the table furnishing those requirements. With such a book of diet tables, a diet can be ordered in less than two minutes for every possible need with amounts of carbohydrate, protein and fat, total glucose and fatty acids, fatty-acid-glucose ratio, heat unit supply per kilo and the total caloric value. Such a book is not only a time saver, but it avoids errors from hasty calculations.

Table 2

DIETS FOR A 70 KILOGRAM (154 LB.) PATIENT
PROTEIN 1.5 GM. PER KILO $\frac{F\ A}{G} = 1.50$

Diet No.	Carbohydrate	Protein	Fat	Total G.	Fatty Acid	F. A. G.	Calories	Calories Per Kilo.
716	3	105	63	70	105	1.50	989	14.1
717	12	105	79	80	120	1.50	1,179	16.8
718	20	105	96	90	135	1.50	1,364	19.5
719	28	105	113	100	150	1.50	1,549	22.1
720	36	105	130	110	165	1.50	1,734	24.8
721	45	105	146	120	180	1.50	1,914	27.3
722	53	105	163	130	195	1.50	2,099	30.0
723	61	105	180	140	210	1.50	2,284	32.6
724	69	105	197	150	225	1.50	2,469	35.3
725	78	105	213	160	240	1.50	2,649	37.8
726	86	105	230	170	255	1.50	2,834	40.5
727	94	105	247	180	270	1.50	3,019	43.1
728	103	105	263	190	285	1.50	3,199	45.7

The ingestion of carbohydrate and especially of sugar increases glycemia of all persons, diabetic or not. If carbohydrate intake be less than 50 gms. daily, acid substances appear in the urine, as in excessive vomiting, toxemia of pregnancy, or cancer of the stomach. Diabetes is merely an advanced form of carbohydrate starvation.

Food yields two products of primary interest to the diabetic: glucose and fatty acids; they have the same effect on the body regardless of whether they are from carbohydrate, protein or fat. Hence the fatty-acid-glucose ratio becomes important.

The $\frac{F\ A}{G}$ ratio which will prevent acid bodies from appearing in the urine varies in different people, even varies in the same person from time to time. But there is a fairly close relationship between the amount of B. oxybutyric acid oxidized and the carbohydrate consumed.

The mathematical scheme for controlling the diet based on Zeller's work and Shaffer's formula offers advantages not secured by any other method. It furnished the basis for computations of the diet tables which I use (*Table 3*). It furnishes a surprise to the physician who is making his first intensive study of food values by directing his attention to the glucose found in fat and it emphasizes a fact that bears repetition for the physician who has studied foods more or less intensively, namely, that both glucose and fatty acids are glucose and fatty acid from whatever source derived.

Such a table makes comprehensible the clinical fact that a diet with a high starch content may yield less glucose than one high in protein and low in carbohydrate. A normal person does not excrete glucose through the kidney when taking starch in any quantity.

Table 3

100 grams of C.H. yields 100 grams of glucose and 0. grams of fatty acid.
100 grams of P. yields 58 grams of glucose and 46 grams of fatty acid.
100 grams of fat yields 10 grams of glucose and 90 grams of fatty acid.

There is some difference of opinion as to the proportion of fatty-acid to glucose that is safe; some hold that a ratio well above that indicated by the relative molecular weights of fat and glucose is safe and use a ratio as high as 3 to 1. It is generally agreed, however, that the diabetic with no acetonuria meets emergencies with a more comfortable reserve. This, coupled with the climatic factor where I work, has led me to keep the $\frac{F\ A}{G}$ ratio below 1.25 until the sugar tolerance is well on the increase.

Maintenance Diet.—In the average case presenting evidences of mild or no acidosis a maintenance diet is selected at the onset. The caloric value and the protein content are determined by the study of the patient physically, the laboratory data and an inquiry into the daily habits. The carbohydrate and fat are figured with only two things in mind: the presence or absence of acidosis and the habits of

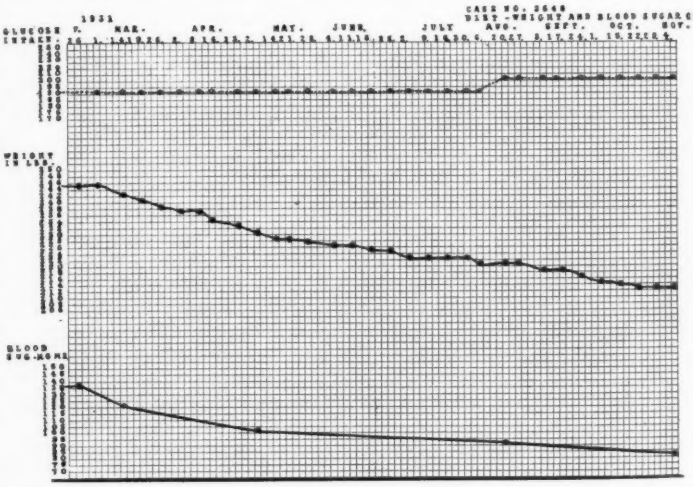

Fig. 1, Case 2648 A

Diet $\frac{FA}{G} = \frac{176}{190}$ ratio 0.90 to August 20, 1931.

Then increased to $\frac{FA}{G} = \frac{176}{200}$ ratio 0.88.

Weight reduced from 245 to 212 pounds. Blood sugar fasting reduced from 135 to 95 mgms. per 100 c. c. of blood. Has continued actively at business with long hours.

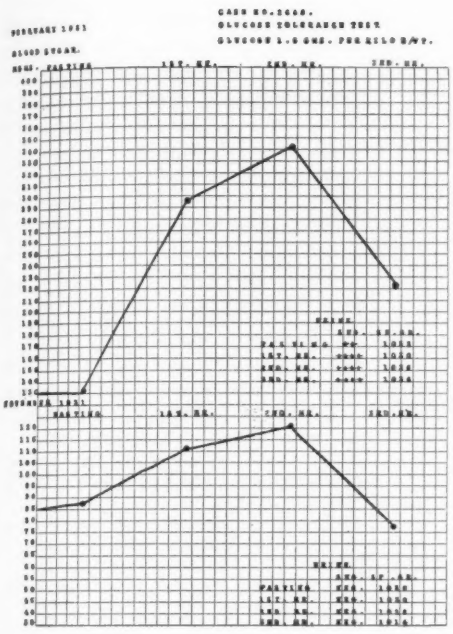

Fig. 2, Case 2648 B

Glucose tolerance curve (upper) February, 1931, showing pancreatic deficiency; normal curve (lower) November, 1931. Weighed diet.

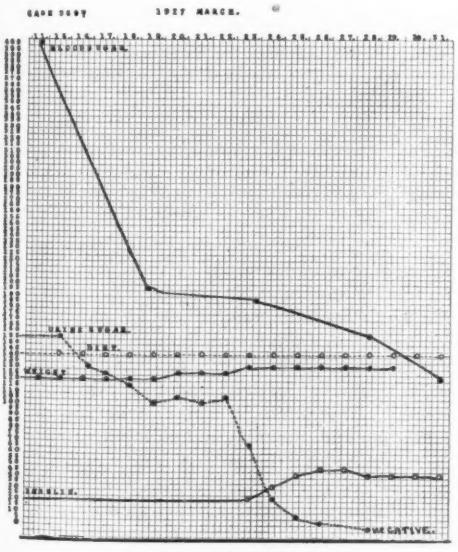

Fig. 3, Case 3597

High blood sugar, high urine sugar loss, normal renal threshold, no acetone nor diacetic acid. Urine sugar loss stabilized before insulin was begun. Note increase in weight.

the patient. These latter are often wrong and some effort at correction must be made, but it should be done gradually. Since one of the desiderata in managing the diabetic is to enable him to live as nearly a normal dietary life as possible, his likes and dislikes must be reckoned with.

Consider *Case 2648A.*—A man weighing 111 kilos is to continue his vocation, that of an attorney, his urine free of acetone, the season winter, his diet habits unusual. A diet (*Fig. 1*) furnishing 2,226 calories (30 calories approximately per kilo normal weight), a protein intake of 90 grams (1.16 gm. per kilo), and a fatty-acid-glucose ratio of 0.90 was selected as a maintenance diet. Such a diet would consist of C.H. 129, P. 90, F. 150, furnishing 190 grams of glucose daily. This diet is not very well balanced, but is influenced by one of the factors which influence budgeting, namely, the patient's diet habits. He had long been using too much carbohydrate and protein, hence this first diet allows a bit higher protein intake than is necessary for sedentary habits, but is still much below his previous daily intake. The two glucose tolerance curves (*Fig. 2*) made at an eight months interval show a diminished islet activity in February with normal function in November. He is yet well above a normal weight, but at the present rate should attain it within

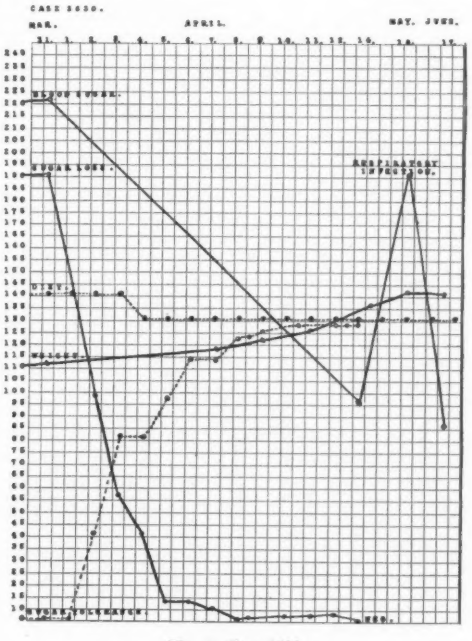

Fig. 4, Case 3630

Moderately high blood sugar, low renal threshold, low sugar tolerance, low grade acidosis. On maintenance diet without insulin blood sugar reduced to normal with gain in weight. Note rise in blood sugar one month later following infection of respiratory system.

Table 4

CASE 41512 A. REDUCTION OF BLOOD SUGAR TO NORMAL WITH INCREASE IN DIET AS APPETITE AND PANCREATIC IMPROVEMENT WARRANTED. NO INSULIN.

Date	Diet in Grams				Heat Units	Fatty Acid	F. & G. Ratio	Urine						Glucose: Intake—Output				Blood		Weight	
	Carb.	Prot.	Fat					Vol. c. c.	Spgr.	React.	Alb.	Acetone	Diac. Ac.	Intake	Loss Per Cent	Loss Total Gms.	Tolerance	Sugar	CO_2	Lb.	Kilo
1930																					
4/ 7	Regular diet							s/s	1018	ac.	neg.	trace	neg.	?	4 plus		?	222	18	132	60
4/ 9	85	60	113	1597	130	1.0		2800	1010	ac.	neg.	2	neg.	130	2.5	70	60				
4/10	85	60	113	1597	130	1.0		1800	1018	ac.	neg.	1	neg.	130	1.	18	112				
4/11	85	60	113	1597	130	1.0		1750	1020	ac.	neg.	neg.	neg.	130	0.5	8.7	121.3				
4/12	85	60	113	1597	130	1.0		2110	1020	ac.	neg.	neg.	neg.	130	heavy	trace	?			132.5	
4/13	85	60	113	1597	130	1.0		2140	1020	ac.	neg.	neg.	neg.	130	heavy	trace	?				
4/14	85	60	113	1597	130	1.0		1800	1014	ac.	neg.	neg.	neg.	130	faint	trace	?				
4/15	85	60	113	1597	130	1.0		1700	1012	ac.	neg.	neg.	neg.	130	neg.	neg.	130	145		132.5	
4/16	Returned home																				
4/29	85	60	113	1597	130	1.0		1500	1010	ac.	neg.	neg.	neg.	130	neg.	neg.	130	130		133	
5/26	91	60	144	1900	140	1.0		1400	1012	ac.	neg.	neg.	neg.	140	neg.	neg.	140			133.4	
7/ 1	91	60	144	1900	140	1.0		1400	1022	ac.	neg.	neg.	neg.	140	neg.	neg.	140	108		133	
8/12	91	60	144	1900	140	1.0		1500	1018	ac.	neg.	neg.	neg.	140	neg.	neg.	140	110		133.5	
10/13	91	60	144	1900	140	1.0		1600	1025	ac.	neg.	neg.	neg.	140	neg.	neg.	140	75	36	133.5	
10/15	109	40	188	2288	188	1.25								150							
	103	60	135	1867	150	1.0								150							

a year; he feels splendidly, is mentally vigorous, and is enthusiastic about his regimen.

Whether the sugar intake exceeds the patient's sugar tolerance is of no concern at this stage of the dietary management. The sugar tolerance can be readily ascertained in such a patient by putting him on the above weighed diet and determining the urine sugar loss daily. The urine sugar loss gradually lessens until it disappears if the tolerance is higher than the intake, or if lower the urine sugar loss will become stabilized in a few days. Such a stabilization is illustrated in *Case 3597* (*Fig. 3*).

The loss of sugar daily at the beginning was 156 grams and it gradually diminished until a period was reached when for four days the average loss was 101 grams daily. The intake was 140 grams, hence 39 grams were being utilized. That is his present sugar tolerance. He needs 140 grams, he oxidizes 39 grams, and the difference is to be burned by insulin. If the difference is small insulin need not be given, as the pancreas function generally rises until, in the majority of cases, the tolerance is on an even keel with the maintenance requirements. Even if the difference be relatively large insulin will not be needed if the urine sugar loss falls rapidly on a weighed diet.

Case 3630 (*Fig. 4*) had shown a glycosuria for a short time only. The urine sugar loss was 190 grams daily on an unweighed diet. On a weighed diet the urine sugar loss fell to 14 grams in five days and disappeared completely in fourteen days. The blood sugar fell from 220 to 95 mgms. during this same period. Such a case does not need insulin. Should the maintenance requirements be increased by additional activity the tolerance often rises with general nutritional improvement and insulin is still not needed. Such a condition is shown in *Case 41512A* (*Table 4*).

When first seen this patient was entirely satisfied on a diet of C.H. 85, P. 60, F. 113, furnishing 130 grams of glucose. A maintenance of weight, which was normal, evidences the accuracy of the diet estimate. After returning home and increasing activity, the diet had to be increased May 26 to C.H. 91, P. 60, F. 144, furnishing 140 grams of glucose daily. The weight continued practically unchanged again indicating a satisfaction of maintenance requirements. With improved pancreas function the diet was again increased on October 15 to C.H. 103, P. 60, F. 135, furnishing 150 grams of glucose. Without insulin and on an increasing glucose intake the blood sugar dropped from 222 mgms. per 100 c. c. of blood on April 7 to 75 mgms. on October 13. This was considered too low, and the diet was again increased.

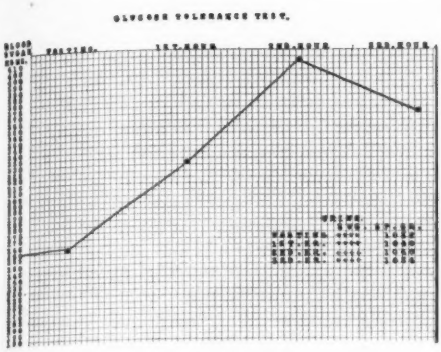

Fig. 5, Case 41512 B

Female, age 52, height 64 inches, weight 132 (60 kilos). Blood sugar fasting 222 mg. Renal threshold about 150. Typical glucose tolerance curve in a diabetic.

The degree of pancreatic deficiency is further shown in this case by *Fig. 5*, which graphically presents the response in the blood sugar to the administration of 1.5 gms. of glucose per kilo of body weight. The blood sugar rose to 330 mgms. at the end of the first hour, rose still higher to 410 at the end of the second hour and dropped at the end of the third hour to 370.

If a patient, again a man, real estate dealer, weighs 50 kilos, is not well enough to attend his office work even a part of each day, has a poor appetite, is acidotic, has a lienteric diarrhea, the season, summer, a diet furnishing 1076 calories (21 per kilo) is selected. This patient, *Case 4729*, fed on a basis of his normal weight of 70 kilos, requires 53 grams of protein (0.75 gm. per kilo; his fatty-acid-glucose ratio should not exceed 0.75. Such requirements are met with a diet of C.H. 72, P. 53, F. 64 (*Fig. 6*).

His carbon dioxide combining power was 20 when this diet was started and acetone 4 plus. The latter disappeared in five days on insulin and the former rose to 38. On Feb. 23, 1931, the diet was increased to 85 C.H., 60 P., 113 F. He remained free of acidosis on this diet which furnished 130 grams of sugar and a fatty-acid-glucose ratio of 1.00 with 1,597 calories daily. Continuing improvement he was put on a diet of 80 C.H., 60 P., 150 F., on March 7, 1931. This furnished 1910 calories and still supplied 130 grams of glucose but a fatty-acid-glucose ratio of 1.25.

Case 3950 (*Fig. 7*) showing a relatively high blood sugar on an unknown diet illustrates an over estimate in dietary needs. A diet providing for 126 gms. of sugar daily with a heat unit intake of 1550 calories was ordered. Four days later this had to be reduced to an intake of 113 gms. daily because of inability to take more. A fatty-acid-glucose ratio of 1.0 was considered allowable, since because of infection and a sugar tolerance on the negative side the administration of insulin was inaugurated at the beginning of observation. A maximum dosage of 62 units daily was found necessary to render the urine sugar free. The sugar tolerance gradually rose from approximately 16 on July 9 to 140 which represents the daily sugar intake on Jan. 7, 1930, when she had been off of insulin for five months. She continued on a weighed diet until August, 1930, and has continued on an approximated diet to date. Her weight steadily decreased until an approximately normal figure was reached. When she went off a weighed diet she was taking 140 gms. of sugar a day with a blood sugar of 78 mgms.

TRAINING THE PATIENT

Either the patient or some member of the family is taught how to figure diets, weigh foods, budget portions, examine the urine qualitatively for sugar, and when necessary, give insulin.

This is a necessity save in very mild cases. *Case 4245* shows a hyperglycemia satisfactorily controlled by teaching the patient how to approximate his helpings. One day's calculation, taken from this patient's record, is shown in *Table 5*.

Some foods permit of satisfactory approximations, but it is obvious that "2 cakes" of sausage permits an elasticity likely to satisfy the most reckless diabetic. How satisfactorily approximations may be done, however, is shown in *Table 6*, where the blood sugar determinations and the weight record are shown. Too frequently such cases gradually lapse into habits

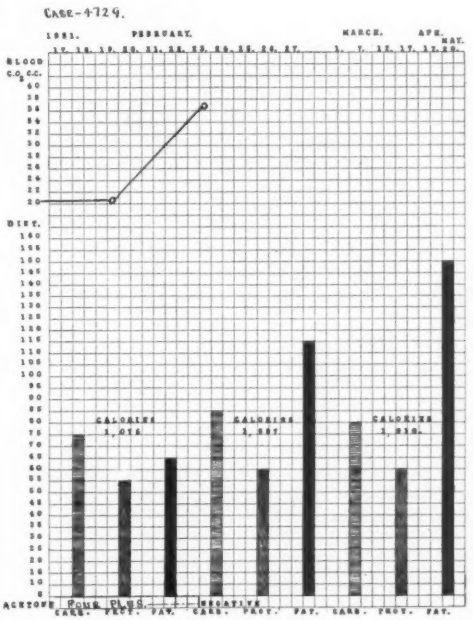

Fig. 6, Case 4729

Male, age 25, realtor. Weight 116, height 70 inches. Disease of seven years' duration, approximated diet and insulin in 1925 and continued for eighteen months. From September, 1930, to February, 1931, lost weight rapidly, digestive upsets, no appetite, sensory nerve disturbances. When seen was acidotic, positive Mantoux, low grade renal insufficiency, greatly discouraged. No change in acetone on diet alone. Urine sugar loss not stabilized before insulin was begun; slow rise in sugar tolerance, no gain in weight.

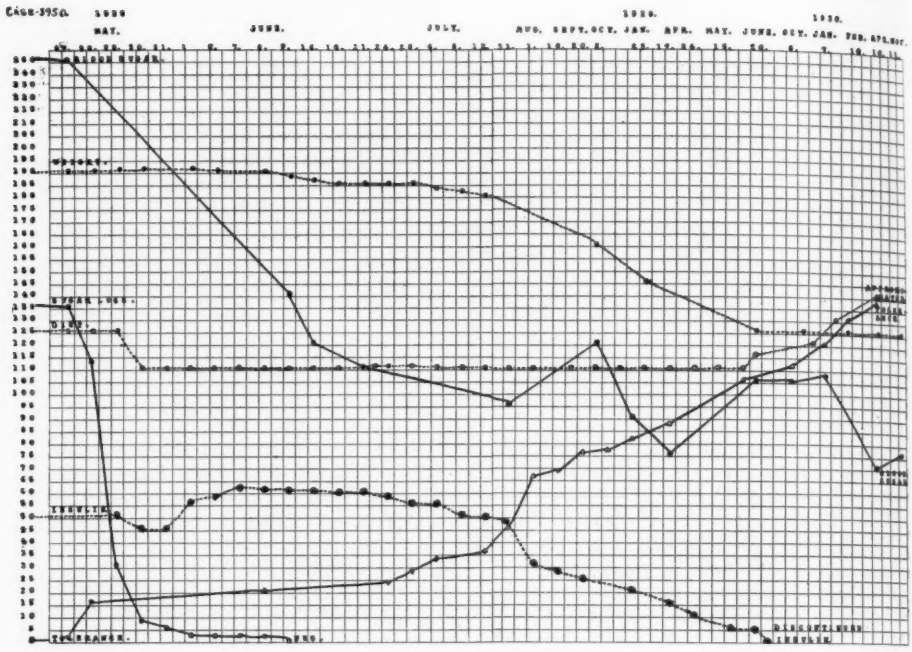

Fig. 7, Case 3950

Female, age 52, height 63 inches, weight 189 (80 kilos). Normal weight 140 (63 kilos). Carbuncle, neck, temperature 103°, Hyperglycemia, glycosuria, acidotic. Maximum insulin dosage 62 units daily. Insulin coefficient 1.6. Has been off insulin since July, 1929. Approximated diet since August, 1930, with a blood sugar of 78 mgms. November, 1930. Note steady increase in sugar tolerance from minus 9 to 140 gms.

Table 5

CASE 4245. LOW GRADE PANCREATIC DEFICIENCY; APPROXIMATE DIET; ARTICLES SELECTED BY PATIENT; AMOUNTS ESTIMATED BY NURSE.

	Gms.	Portions	C.H.	P.	F.
Breakfast:					
Oatmeal (dry wt.)	15	4 tablespoonsful cooked	10	3	1
Cream 20 per cent	120	8 tablespoonsful	4	4	24
Bacon (cooked)	15	3 slices	0	3	8
Toast (white)	15	1 thin slice	9	2	0
Butter	5	1 pat	0	0	4
Lunch:					
Pork sausage	60	2 cakes	0	10	30
Potatoes (fried)	60	4 tablespoonsful	12	2	10
Rye bread	30	2 thin slices	11	4	0
Rhubarb (sweetened with saccharin)	120	8 tablespoonsful	4	2	0
Canteloupe	130	½ small melon	12	0	0
Butter	10	2 pats	0	0	8
Dinner:					
Lamb (roast)	60	Medium helping	0	16	10
Peas (green)	60	4 tablespoonsful	2	1	0
Waldorf Salad:					
Apple	25	¾ medium size	4	0	0
Lettuce	30	4 leaves—medium	1	1	0
Pecans	30	2 tablespoonsful	2	1	11
Mayonnaise	18	1 tablespoonful	0	0	18
Celery	60	6 hearts	2	1	0
Rye bread	30	2 medium slices	11	4	0
Buttermilk	210	1 glass (oz. 7)	10	7	0
			94	60	124

FA═140═1.00 Calories 1722.

G 140

Table 6

CASE 4245. SHOWING BLOOD SUGAR REDUCTION FROM 198 MG. TO 120 MG. IN 3 MONTHS AND 3 WEEKS. NOTE MAINTENANCE OF WEIGHT.

Date	Blood Sugar	Weight
April 3, 1931	198 mgms.	177.5 lb.
April 28, 1931	140 mgms.	174 lb.
May 26, 1931	150 mgms.	174 lb.
June 16, 1931	140 mgms.	171.5 lb.
July 28, 1931	120 mgms.	172.5 lb.
October 27, 1931	125 mgms.	176.5 lb.

Urine negative for sugar since April 28, 1931.

of indulgence and require the regimen of a weighed diet. I am convinced that a greater likelihood of following instructions obtains when the patient is taught food values, watches urine sugar disappear and blood sugar return to normal. He obtains a close-up of the disease, observes the effect of accuracy, is impressed by the approach to mathematical control and the influence of such experience is more lasting. He comes to doing a thing because he comes to understand why the thing should be done instead of merely acquiring a habit of taking orders. There was a time when violation of dietary orders was the rule rather than the exception; now, such violation is the exception rather than the rule. I now obtain more intelligent cooperation from my diabetics than from any other class of chronic diseases.

I am frequently asked how long it takes to teach a layman what the diabetic should know about diet. The time varies with the individual, but he can become trustworthy in one week. Age is no factor. One of the best trained patients I have had was eight years old and we are training one now at 70. Often the whole family learns how to figure the patient's diet; many wives, themselves obese, have applied the dietetic principles to themselves and been made happy in attaining a more slender figure; the maid or cook not a few times has been taught how to carry on.

I prefer to keep my diabetics in their homes if they live in the city. If they are sent in from outlying districts or other states I prefer to have them go to housekeeping in a small furnished apartment. I find this plan far more preferable to having them in a hospital. They are thus living under conditions not unlike those that will obtain on returning home. They order from the grocery what they want to eat; they learn the lesson from the practical application. I have been reminded by some of them of the analogy of our plan to the methods of old Squeers in Nicholas Nickleby. Be that as it may, the patient, whether a man or child, accompanied by some female member of the household, living in his temporary home, is visited daily by my nurse and taught in his own kitchen how to calculate and prepare his food. This plan has the added advantage over hospital care of permitting the patient to select his own food. The vegetables he likes may be chosen. (Much of the hospital food as purchased is canned. One can understand this during winter months, but it is incomprehensible during the season of vegetable and fruit plentitude.) In the average hospital, supervising nurses are not familiar with dietetic principles and the dietitian does not find the time to train the patient. Therefore, my own office force takes over the training. And who denies that enthusiasm is contagious?

In figuring a diet something depends on the method. *Case 2686* has his diet figured by his wife. The figures at the top are my contribution; they are the wife's bank account daily for her husband's food. As she sets down each food she determines the amount he is to eat at that meal and then computes its value in terms of carbohydrate, protein and fat. She continues her budgeting until the evening meal is made out when she finds the day's allowance has been utilized. She has neither overdrawn her account for the day nor has she been miserly and hoarded. A diet for one day was photographed from the book of diets that have been figured for this patient (*Fig. 8*). Each day varies with

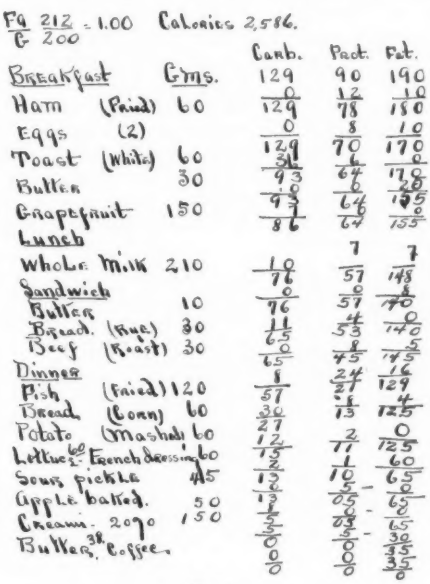

Fig. 8
Example of diet as figured by patient. The menu is his own selection.

his desires limited only by the season and the family purse.

It is sometimes urged that such daily budgeting is time consuming and annoying. Do people tire of writing their menus at the mountain or seashore hotel? They like it rather jolly well. It is also urged that folks tire of weighing foods. Not if they realize the necessity. Does the butcher grow negligent about weighing his cuts, or the coal dealer get weary with weighing his run of the mine? The business of getting well is as important as butchering for profit or merchandising coal for a livelihood. I am persuaded that the lukewarmness emanates not infrequently from the patient's medical counselor who has been too indolent or too busy to equip himself to instruct. How often have I heard the order to the supervising nurse in the hospital "Put this patient on a diabetic diet." If physicians would only learn that there should be no such term in diabetic management; that the diabetic may eat any single food which any normal person may eat, that only quantity is at issue, how much happier would be the lot of the one million diabetics in this country!

The little girl of eight figured her diet for a day for a group of doctors at one of my clinics. One asked why she selected rye bread. "Because I get more of it," came the answer quickly. While patients are yet hungry, early in the management, it is interesting to watch how soon they learn to figure their food to afford bulk. As the tolerance approaches normal, or after insulin is started, this necessity no longer confronts them. I often have patients tell me when I first see them that they never eat potatoes or white bread or corn. When they are taught food values and how to balance diets they may have the satisfaction of eating anything they desire.

DIABETIC FOODS

I do not use the so-called diabetic foods. They are expensive, often unpalatable, sometimes difficult of procurement for the rural diabetic, and not of uniform composition. One must have the analysis of each bread at hand if he expects to figure accurately its value in the day's dietary. The analysis furnished by the manufacturer may be accurate; it may not. The physician does not know nor can he verify it. True, the "Report of the Connecticut Agricultural Experiment Station" furnishes an authoritative analysis of these foods, but is not recent enough to cover the vintage of the past few years. A casual study of the analysis of the foods covered in that report should be enough to convince one of the futility of using them. A few taken at random are shown in *Table 7*. The variation of nitrogen and starch is much greater than that obtaining in wheat bread, corn bread and rye bread.

If no sugar is furnished by the food as is the case with some of the soja bean flours, then why eat it? Better fill the stomach with the 5 per cent vegetables. If as much as 72 per cent of starch is furnished in many of the gluten flours, then the sugar available is equal to wheat flour, baker's grade. Further, all of the gluten flours contain protein, some as high as 76 per cent, and 58 per cent of this becomes available sugar. The fat content of these diabetic breads is as variable as the sugar content and in the acidotic patient the fat becomes of more moment than the sugar. When one considers the varieties of gluten flour, the impossibility of

Table 7

ANALYSES OF FLOUR, MEAL AND BREAD FROM REPORT OF THE CONNECTICUT AGRICULTURAL EXPERIMENT STATION. BULLETIN 220.

Name	Manufacturer	Protein	Starch	Calories
Gluten flour	Barker	76.9	2.5	361
Gluten flour	Empire	13.11	59.0	361
Gluten flour	Farrell & Rhines	9.9	72.0	349
Gluten biscuit—40 per cent	Kellogg	40.9	35.5	364
Gluten biscuit—80 per cent	Kellogg	75.1	4.7	355
Casoid biscuit—No. 1	Callard & Stewart	63.0	8.1	440
Casoid biscuit—No. 2	Callard & Stewart	58.1	0.0	—
Almond biscuit	Johnson Educator Company	29.0	50.0	412
Almond biscuit	Callard & Stewart	28.3	36.8	512
Almond meal	Health Food Company	50.6	7.2	407

harmonizing these breads for practical use becomes apparent. There is pure gluten flour, pure washed gluten flour, self-rising gluten flour, imported gluten flour, special plain gluten flour, standard gluten flour, and just plain gluten flour. The clinic would have to be motorized to carry the analyses of the gluten nonsense alone. Casoid, soja bean, soy bean, almond and scores of others give evidence of manufacturers' activity, salesmen's urbanity, physicians' credulity, and patients' gullibility.

SUMMARY

What is a normal diet for a normal person is a question permitting of some latitude in determination. In so far as one is able to determine dietary normals, such normals should constitute, in the main, the diet of the diabetic. The diabetic is entitled to live as nearly a normal dietary life as his disease permits, hence:

Extremes in diet values are not advocated for the diabetic.

The individual method of handling diabetics and their diet is discussed. Especial emphasis is placed on training the patient or some member of the family.

Diabetic foods, so-called, are discussed and their use discouraged.

DISCUSSION (*Abstract*)

Dr. J. S. McLester, Birmingham, Ala.—I think we all agree with Dr. Simpson that the diabetic diet should be a simple one, such as people ordinarily eat, and that freak diets are a mistake. It is important to give the patient food such as the other members of the family eat, the foods which are usual to his station of life. It is a mistake to force a patient to weigh his food at every meal. Life is hardly worth living when you have to weigh everything you eat.

Dr. Isaac I. Lemann, New Orleans, La.—We have believed from the time when we first had insulin that we need not keep our patients on a diet that was entirely disagreeable to them. When insulin made its appearance we were under the influence of the school of thought which said that we must keep down not only the protein, but the carbohydrate intake, and in order to maintain the patient in any kind of health we had to run up the fat to very extreme levels. That was a distasteful diet, a diet that the Eskimos find palatable, but not people in the temperate zone. There is no longer any reason for such extreme diets as those, and even in the early days of insulin, as far as we were concerned, we laid down a dead line beyond which we would not go in restricting the carbohydrates. That dead line has gradually risen, and while I do not find myself in accord with the extreme views of Sansum, I do feel there is no reason to keep a patient from having a considerable amount of starch in his food, not sugar, but carbohydrate. That level of carbohydrates has risen since the early days of insulin from 50 to 60 grams to 100 or 125 grams.

We should make the dietary regulations as simple as possible. We should make them fit the usual habits of the patient.

We who are handling diabetics have made too much of a mystery of the matter of dealing with them, so that the reaction of the profession at large has been to regard diabetes as a sort of *noli me tangere*. "You have diabetes, you had better go to a specialist." There are too many diabetics in the United States for the specialists to care for. It is a problem for the general practitioner. Hence, the general practitioner must learn to take care of the usual case.

We should not give too much consideration to the relation of fatty acids to glucose and to very elaborate calculations. What we must remember in the patient's diet is that he must be kept slightly under-nourished. At least, he must not be allowed to get over fat. The under-nourished person we must cause to increase in weight; the over-nourished person we must cause to decrease in weight. Having determined what we are going to do with the particular patient, with regard to his habits of life, with regard to his nutrition, and with regulation of the protein, (not exceeding 0.75 gram of protein for each kilo of body weight), we can, with some very simple rules, adapt the diet to the patient.

I think it is good discipline for the patient to weigh the food. It is good discipline in severe cases of diabetes to continue that weighing for a long time. There are no patients who continue indefinitely to weigh their food. I insist from time to time that patients test their diet by weighing what they are eating. It will suffice if they do it once a month, or once in ten days, to see that they are not grossly exceeding their allowance.

Dr. M. Jay Flipse, Miami, Fla.—Joslin and others have called attention to the blood cholesterol and its importance in the prognosis of diabetes; also the relation between the high blood cholesterol and premature arteriosclerosis.

In spite of the fact that insulin has been in use some ten years, there can be as yet no standardized method for the treatment of diabetics. Many of the factors in diabetes are still undetermined and individual patients appear to vary greatly not only in the degree of diabetic disease, but also in their ability to handle fats and carbohydrates.

In connection with Dr. Joslin's work, there appeared to be considerable value from the estimation of the blood cholesterol, as well as the blood sugar. Until the high cholesterol values have been proven to be of no significance, the reduction in cholesterol should be accomplished as well as the reduction in glucose.

EMOTIONAL INSTABILITY AS A FREQUENT CAUSE OF DIGESTIVE DISORDERS*

By JAMES S. MCLESTER, M.D.,
Birmingham, Ala.

Of the patients who come to the physician complaining of digestive disturbances approximately one-third have no recognizable disease of the abdominal organs. They are the so-called neurasthenics; and to me they present in ever-increasing proportion the greatest single problem of clinical medicine. After a mature study of these patients, undertaken in a sympathetic endeavor to understand not only the character of their distress but also the nature of its underlying causes, I have gained two lasting impressions: first, that emotional instability is of enormous influence in the production of their disabilities, and second, that this lack of stability is inherent in the patient. His troubles are not due to external causes, they are of the warp and woof of which he is made.

When we contemplate the life history of such people, their illnesses, their reaction to the incidents of everyday existence, big and little, and the way they meet the vicissitudes of life, and then inquire into the character of their antecedents, we are forced to the conclusion that they are not the victims merely of fortuitous circumstance. They are born, not made, neurasthenics; the situations in which they chance to find themselves are of distinctly subordinate influence. True, domestic trials, business worries, or unfortunate environment may have a contributory effect, but the real trouble lies deeper. It is, as I see it, an inborn lack of balance which from the beginning has predestined its victim to trouble. The nervous system of this type of patient may be likened to a substandard automobile tire. Both the patient and the tire are made of poor fabric and almost any shock will cause a blowout. We are tempted to attribute the blowout to the immediately preceding shock, but the real reason is defective material. We can patch up the tire and likewise we can patch up the patient, but thereafter the staunchness of both is questionable.

Wherein lies this defect? Is it faulty function of the glands of internal secretion? Is it psychic in origin? Does it represent a lack of balance of the vegetative nervous system? Or is it merely one feature of a general constitutional inferiority? This question is clearly hard to answer, but in the patients of whom I write, whatever other systems are at fault, it is evident that the picture is dominated by derangement of those functions which are controlled by the vegetative nervous system. Fibres from this system form a part of a nicely adjusted, well-coordinated motor mechanism, to which the motility of the bowel is subservient, and any disturbance of this innervation is apt profoundly to upset these motor functions. The complaints of the gastro-intestinal invalid can most often be traced to disturbances of this character and, since these people show additional evidences of nervous imbalance, it seems reasonable to conclude that their troubles are, in large part, dependent upon an instability of the vegetative nervous system.

The symptoms are innumerable. They may suggest nothing, or, on the other hand, they may simulate almost any disease, not the least frequent among which are tenderness in the lower abdomen suggesting appendicitis, hunger pains simulating gastric ulcer, or the abdominal distention of gall-bladder disease. These discomforts are not a mere figment of the imagination. They are real. True, the patient, in his extreme sensitiveness, may grossly exaggerate the extent of his discomfort, or he may become acutely aware of physiologic processes that in the rest of us never rise to the threshold of consciousness, but in most instances there is genuine disturbance of function, usually of intestinal tone and motility. It is of this last that many patients complain most grievously. As striking evidences of such disturbed neuro-muscular control, witness the vomiting of seasickness or that which accompanies a nauseating sight, the diarrhea of excitement, and the constipation which is experienced aboard ship. Such disturbances are of brief tenor, but we could also cite equally profound, though less graphic, derangements of long duration. In this last category could be placed mucous colitis and the somewhat milder disorder of similar nature called irritable colon, as well as the abdominal distention, sometimes with the noisy belching of gas, of which many patients insistently complain. I know of nothing more typical of the disturbances of which I write than this last symptom.

Roentgenologic studies of these patients frequently reveal nothing abnormal. At other times a fairly characteristic picture is presented, such, for example, as the excessively motile stomach

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seen in migraine patients, or the smooth redundant colon, spastic in one segment and relaxed in another, and relatively free of haustra, seen in mucous colitis. These last appearances in a less distinct form, that is, elongation of the colon with smoothness of outline, are fairly frequent and seem to be significant.

It is not, however, upon the radiologic appearances or upon the nature of the abdominal distress that chief reliance should be placed, for of vastly greater importance is the composite clinical picture. To the alert physician, who is willing patiently to listen and to observe, the patient's personality and emotional pattern, which is revealed in the taking of the anamnesis, more nearly tells the story than anything else. The manner in which he recites his troubles, his facial expression, the intensity of his interest in his symptoms and their extreme gravity to him, the number of physicians whom he has consulted, and, not the least among these, the little memorandum which he produces, all are significant. I am so convinced of the importance of the information to be obtained from a study of the patient's personality that if I were forced to restrict myself to one of the several diagnostic procedures commonly used I would choose invariably to take the history, and would delegate to someone else the physical examination and other procedures. For the sake of thoroughness, and also that the patient may know that his troubles are receiving full consideration, these other diagnostic procedures should in no part be omitted, but to the physician who is experienced in his dealing with these people, the diagnosis usually becomes evident as he observes the patient's manner and looks into his face while he tells of his woes.

What can be done for these unfortunates? A great deal. Too often, when it is realized that their troubles are due in large measure to an inherent defect which is a fixed characteristic of the individual, the physician assumes a fatalistic attitude and no sustained effort toward treatment is made. This attitude is not justified. I am convinced that with patience on the part of the physician and confidence on the part of the subject a great deal can be accomplished. Much, however, is required of the physician who would deal with such patients successfully. Not only must he have patience and the ability to appear unhurried, no matter what the pressure, but he must have tact, genuine interest and a fair understanding of the nature of the trouble, together with an ability to transmit this understanding to the patient himself.

The first thing the patient needs is reassurance, and then an explanation suited to his intelligence. He should be told frankly but tactfully that his psychic and emotional characteristics are his own and that we can no more change them than we can change the color of his eyes, that each of us has his handicap in life and that his is an unstable nervous system. He should be taught to recognize that, because of this handicap, he has his limitations and that he must learn, contentedly and without fretting, to live within them. He should be given to understand that abnormal nerve impulses resulting in disturbances of function can be accentuated or inhibited according to the state of the mind and the play of the emotions, and that if in his discomfort he becomes anxious or frightened everything will be worse, but that if he can teach himself to develop poise and a don't-give-a-damn feeling, then things will be better. He should be comforted by the assurance that when this has been accomplished and he has achieved some degree of mental equilibrium then many of his ills will vanish and a modicum of happiness will come.

It is well, too, to remind him that a person's perceptive powers may become so acutely sensitive as to render him painfully aware of normal physiologic processes which ordinarily do not thrust themselves upon our attention, such as the beating of the heart, the pulsation of the aorta, or the movements of the stomach and intestines, and to admonish him that when such sensations disturb him it is only by disregarding them that he can finally escape. I frequently illustrate this by recalling our childhood days when for a few days each fall the heavy woolen underwear just put on scratched terribly; after this, it scratched no more. The wool remained just as "scratchy," but it was ignored and soon it no longer intruded itself upon our consciousness. If the neurotic patient can be taught in like manner to ignore the many discomforts which beset him, great progress will be made.

These patients all want a special diet. It is of importance first to overcome their various phobias and to teach them that they can with impunity eat a simple, well-balanced diet such as is suitable for anybody. True, this is a task which oftentimes can be accomplished only in a hospital with the constant reassurance and moral support of both physician and nurse, but it can be done.

Too much thought in the selection of food is bad for neurotic persons, but in one particular a certain degree of restriction is sometimes necessary. Being acutely subject to suggestion, these patients usually accept at its face value all of the extensive propaganda for vitamins and roughage seen in the current literature, and, in the belief that this is wholesome, most of them have acquired the habit of eating large quantities of roughage, notably of bran and whole wheat bread. This is a mistake. Many such persons are peculiarly sensitive to roughage, which, if taken in large quantities, will accentuate their discomforts; remarkable relief will be obtained if they are restricted to a smooth diet, consisting largely of milk, cereals, white bread, butter, potatoes, rice, eggs, and tender meats. In prescribing such a diet, however, it is necessary to add orange juice, tomato juice, and other vitamin-carrying smooth articles, and also in order to give the intestinal contents the necessary bulk and consistency, to include plain agar in rather large quantities.

Should these patients be given sedative drugs and other medicines? This question cannot be categorically answered. It can be answered only by the physician according to what he sees in the patient. Drugs as a rule should be avoided, but sometimes a mild sedative given for a brief period will have a wonderful effect in allaying the patient's anxiety and in making him more comfortable, which in turn will render him more receptive to the advice offered by the physician. This is particularly true when vascular hypertension is a complicating feature, for in such cases small doses of chloral frequently exert a happy and lasting effect. Likewise iodine is helpful in those many borderline cases which appear to include a mild degree of hyperthyroidism. There are many other drugs and methods of treatment, particularly hydrotherapy, physiotherapy and various hygienic measures, which the discriminating physician will use in selected cases, but these are of vastly less importance than psychotherapy. The physician's approach, his attitude, and what he says to the patient alone most often make for success or failure.

Finally, the faculty for helping neurasthenic patients is not without its penalty. If we benefit them, they continue to return for further moral support, and properly so; then others of this same ilk come, and if the physician's efforts are still rewarded with success, soon his entire time is consumed with long conferences. There remains little time for anything else. To obviate this, the physician must learn properly to gauge the amount of time he can afford to give each patient and then, without the least letting down of interest, and without any appearance of hurry, skillfully to terminate a conference which might otherwise be well-nigh interminable. To do this successfully is the acme of accomplishment.

DISCUSSION (*Abstract*)

Dr. Allan Eustis, New Orleans, La.—I wish my remarks to be construed not as criticism. I wish, however, to caution the profession against going too far on the psychological side at the expense of the physical examination. I understood Dr. McLester to say that he prefers to take the history and leave the physical examination to someone else. We know him well enough, however, to feel certain that he does not leave the examination to any Tom, Dick or Harry, and that he checks up on this also.

At this time I have a patient in Touro Infirmary, who for fifteen years has been treated as a "neurotic." An x-ray of the sinuses shows the sphenoid to be very much involved. With this she has a spastic colitis and other conditions that go with it. I simply mention this case as proof that the best of us may make mistakes in laying too much stress upon the neurotic side.

A large number of these cases I find associated with severe intestinal absorption and a vicious cycle occurs. While no conclusive experiments have been carried on, it is rational to believe that the alkaloids absorbed from the intestinal canal have some effect in stimulating reflex excitability. Some experiments which were conducted by me about twenty years ago seem to bear this out. Little stress was laid upon my results, as they were carried on in conjunction with other work. I was interested in attempting to produce asthma in guinea pigs with injections of sterile human feces. I was impressed with the frequency with which these guinea pigs became irritable. Two sets of guinea pigs were injected daily, one set with physiologic salt solution and the other with extract of human feces.

In a few weeks those injected with extract of human feces, when laid upon the table, would jump when the table was tapped. If the hair were lightly pulled, they would jump away and cry out, while those injected with salt solution remained passive.

Along with a psychological study of patients, a thorough study of the intestinal condition should be made.

Dr. W. A. Dearman, Gulfport, Miss.—We pay, as a rule, very little attention to the autonomic nervous system.

It is taken for granted that Dr. McLester works his cases up thoroughly, and certainly he would not overlook a blood study or a thorough study of the gastrointestinal tract. I am inclined to agree with him that, after all these investigations have been made, then the story and the answer to the question may be found in the instability of the autonomic nervous system.

The autonomic nervous system is a nervous system that is self-controlled. It is independent of the cerebrospinal nervous system, inasmuch as the nerve supplies do not arise directly from the cerebrospinal nervous system. It is a set of nerves that arises from the gray substance.

The autonomic nervous system supplies all the endo-

crine glands. This is why we have a thyroid disturbance not infrequently in instability of the autonomic nervous system. It supplies the viscera, blood vessels, and every organ having involuntary muscle tissue.

One-third of our cases possibly will come in this class. I doubt that there is a physician in my presence who has not had at least one or more of these patients. They require frequent examinations; they go from the Canadian line on the north to the Gulf on the south consulting physicians. I have always thought that every patient should be given a history of his case, what was done, the diagnosis made, the treatment employed, and the progress made, to carry with him so that when he went to another physician there would not be all this work to be done over again.

An unstable, or unbalanced, or an improper functioning of the autonomic nervous system is based on intrinsic factors, on a familial tendency, probably hereditary, congenital, and probably never acquired. These patients have an unstable nervous system, are born with it, have it when we see them, and probably will have it all their lives. Possibly they will get better, but they will be prone to have recurrences. I call them fixed motor invalids. The spells pass off and we pay very little attention to them. We can do them little, if any, good; still there is hope.

The autonomic nervous system may be a perpetual source of disorder. In some cases there is continuous discomfort, in others there are violent storms, chiefly occurring in the gastrointestinal tract. Many cases have been operated upon for acute appendical colic, biliary colic, or ruptured gastric ulcer. This type of patient is likely to go the rounds of surgeons and come back to the psychiatrist and internist, operated upon until he is a human wreck. The autonomic nervous system, when it becomes unstable, may give rise to all kinds of disorders.

We speak of intrinsic factors. I think extrinsic factors should also be considered. I always stress in my history how much alcohol, coffee, tea, drugs, and tobacco are being used. You would be surprised to know how many people are smoking forty cigarettes a day and drinking twenty coca-colas.

The treatment is preventive, palliative, and remedial. Rest, physical and mental, the correction of eyestrain, kidney ectopia, visceroptosis, uterine displacements, and foci of infection, will put the patient's feet off the low grounds of sorrow and despair and probably plant them upon a highway of recovery and well-being.

Dr. John L. Jelks, Memphis, Tenn.—I should like to ask Dr. McLester whether he looks into the sigmoid in spastic cases, after the intestine has been thoroughly washed out, if you please, not with an enema, but with a good dose of Epsom salts, which, as you know, has a tendency to relieve spasm and not create it. Spastic and dilated, alternating areas, will be found either with the x-ray or with the sigmoidoscope, and in many cases you cannot introduce the sigmoidoscope without first applying magnesia, which has the same effect as in the duodenum.

Patients with visceroptosis, uterine displacement, copremia, and low metabolism go from physician to physician unless a thorough and exhaustive study of them is made. Unless you clean the upstairs of focal infections you are not going to clean the colon in those cases.

Dr. McLester (closing).—I am afraid I created a misunderstanding. I intended to say that no part of the usual diagnostic procedure should be omitted, but if I were forced to confine myself to one procedure and to delegate all others to someone else, I would choose to take the patient's history.

THE USE OF THE MODIFIED ASCHHEIM-ZONDEK TEST FOR PREGNANCY*

By H. L. KINCAID, M.S., M.D.,
and
H. J. RAFN, B.S., M.S.,
Houston, Tex.

It is not the purpose of this paper to discuss the literature on the subject of the Aschheim-Zondek test and its modifications, or to detail the biologic basis upon which it depends. Since Aschheim and Zondek's pioneer work, reviewed by Aschheim,[1] which is the basis upon which all tests using the action of the hormone of the anterior lobe of the pituitary depends, many workers have confirmed the fact that pregnant women excrete large amounts of this hormone in their urine. In 1929, Freidman,[2] because the rabbit does not ovulate except after copulation, injected into the blood stream of female rabbits urine from 18 pregnant women. All of these rabbits showed well developed corpora hemorrhagica, while 14 specimens obtained from non-pregnant women did not produce any changes in the ovaries. Since that time many investigators have confirmed this fact and this modification, because of its greater simplicity and more rapid action, is likely to supplant the original Aschheim-Zondek test which depends on the use of mice. Later Freidman and Lapham[3] reported the results of 92 tests in which the laboratory report agreed with the clinical findings.

The accuracy of these findings has been further confirmed by Magath and Randall,[4] who injected urine from 85 patients, 38 of whom were pregnant and 47 non-pregnant. They had one false positive. One rabbit showed corpora hemorrhagica, the patient not being pregnant. There was a possibility that this rabbit had

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*From the Department of Obstetrics of the Houston Clinic.

copulated. One specimen from a pregnant woman did not produce ovulation in the rabbit, but when the injection was repeated five days later the test was positive. Reinhart and Scott[5] injected urine from 50 patients. Forty-nine of these checked with the clinical findings, one being a false negative. Schneider[6] reports the results in 100 patients, 50 controls and 50 test cases, the clinical and laboratory findings agreeing in every instance.

Being impressed by the article of Freidman and Lapham,[3] we decided to study the practical value of this test in the early diagnosis of pregnancy under the ordinary circumstances of private practice. With the exception of six control urines, these tests represent the problems of diagnosis occurring over a period of three months. We felt that sufficient data had already been accumulated regarding the reliability of the reaction.

Technic.—While investigators vary somewhat in the amount of urine used, the least being 5 c. c. by Freidman[2] in his original experiments, most workers used between 5 and 15 c. c. in a single injection. Freidman and Lapham[3] used 24 c. c. divided into 6 injections over a forty-eight hour period. Some workers read the results in from eighteen to thirty hours; apparently, however, the test can be read in twelve hours with equal success.

Some men recommend only sexually mature rabbits while others prefer those between twelve and fourteen weeks of age. The immature rabbits are not apt to show corpora hemorrhagica because of copulation; hence do not need to be kept isolated as is necessary with sexually mature ones. The workers who advocate sexually mature rabbits contend that the immature ones may show false negative results because of the immaturity of the ovary. We felt that the safer procedure would be to use mature animals, especially since our rabbits had been isolated for more than one month prior to their use. We varied the amount of urine somewhat, from 10 to 20 c. c., and waited from twenty-four to forty-eight hours before reading results.

The ear vein was selected as the site of injection, which was used by all workers, except Wood,[7] who injected directly into the heart under anesthesia. A filtered morning specimen was injected as soon as possible after collection. No sterile precautions were used, as all workers agree that this is unnecessary.

Results.—A total of 66 rabbits were injected. Eight specimens were too toxic and the rabbits died. This is a rather high mortality, as Freidman and Lapham[3] found only three too toxic out of 108 rabbits used. Most of these fatalities occurred during one very bad heat wave, which may have some bearing on the mortality. We used only 6 controls; four known pregnant and two known to be not pregnant, the laboratory report agreeing with the clinical data in five instances. The sixth patient was twenty-one weeks pregnant, but the urine did not produce any change in the ovaries of the test animal. The remaining 52 rabbits represent tests done on the urine of 47 women in whom the diagnosis of pregnancy could not definitely be determined clinically.

The clinical data and the laboratory findings agreed in 39 instances, 21 of these women being pregnant, and in each instance the rabbits showed fresh corpora hemorrhagica in the ovaries. The remaining 18 gave a negative laboratory report and subsequent examinations showed all these patients not pregnant.

The following histories illustrate how the test can be used in the diagnosis of doubtful cases:

Case 1.—A nurse, age 24, had been married three years, with no pregnancies. Menses the previous month were normal. Three weeks later she began to spot with cramping pains in the right side for three days prior to examination. Examination showed a normal cervix, uterus not enlarged, but a small mass felt in the right tubo-ovarian region. Urine was injected into two rabbits, both of which gave a positive reaction for pregnancy. Laparotomy the next day disclosed a right tubal abortion.

Case 2.—A business woman, age 41, with one child 18 years old, came to the office because she had missed a period three weeks earlier. There were no other presumptive signs of pregnancy. Examination showed an enlarged uterus, slightly softer than normal, with several fibroids subserous in type, varying in size from a walnut to a small orange. It was impossible to be positive about the pregnancy, although it seemed unlikely. Three rabbits were injected over a period of two weeks and all showed corpora hemorrhagica. Reexamination was still indefinite. Two gynecologists saw the patient in consultation, one believing that fibroids were the cause of the enlargement, the other adding to that diagnosis an ovarian cyst. At laparotomy a three months' fetus was found in a uterus containing many fibroids, both subserous and intramural, making hysterectomy necessary.

Case 3.—A housewife, age 26, married, with one child, stated that she had decided to become pregnant again. The menses were always regular. Believing that if conception took place following menstruation she would have a boy, she tried after the next period. Three weeks later we collected a specimen of urine, which produced corpora hemorrhagica when injected into the rabbit. The next period the patient menstruated very little, and from all evidences we can gather at this

time, this test was positive three weeks following conception.

Case 4.—A housewife, age 28, married, with one child, had been having considerable menstrual disturbance for the preceding several months, the periods lasting two to three weeks. This time she had passed her regular time one week, and when seen she was having cramps at three to five minute intervals, which she described as exactly like the pains of labor. The uterus could be palpated above the symphysis and on bimanual examination was enlarged to the size of a three months pregnancy. Although the cervix was hard, the uterus felt exactly like a pregnancy in spite of the fact that she gave a history of bilateral salpingectomy several years previously. The rabbit injected showed no corpora hemorrhagica and later the patient passed several large clots with no evidence of decidual tissue. The diagnosis was hematometra.

Case 5.—A housewife, age 38, para 3, went past her menstrual date one week. Examination rather favored the diagnosis of pregnancy, but the rabbit was reported as negative. Later the patient began cramping and bleeding as if she were aborting. However, no decidual tissue was passed and in a few days she had entirely recovered.

Early in our experience we made two mistakes in reading the laboratory results. In one instance the corpora hemorrhagica appeared to be old, but eight days later we repeated the test and made a diagnosis of pregnancy which was later confirmed clinically. In the other instance we reported the rabbit as negative, seeing only one small atypical hemorrhage. Evidently we were in error, as the woman later was found to be pregnant.

There remain to be discussed six women whose laboratory report did not coincide with the clinical findings. Three of these women gave a false positive reaction under the same circumstances. Two of them were three days past their calculated menstrual date and the urine, when injected into rabbits, produced typical hemorrhagic areas. Both these women menstruated normally two days later and have had no subsequent menstrual disorders. The third was exactly like these two except that she was past due five days and had a regular period five days later.

The remaining three instances of inaccuracies of the test occurred in women known to be pregnant, whose urine did not produce corpora hemorrhagica in the rabbits. One woman was eight weeks pregnant, the second was one week past her regular menses and later examination showed her pregnant. In the third instance two specimens were used, one at the fifth week of pregnancy and the second three weeks later, both tests being negative.

DISCUSSION

It seems to us that there can be two explanations for the three false positive reactions we obtained. Fluman[8] has shown that there is a variation in the amount of anterior pituitary hormone in the blood of women having irregular menses. Mazer and Hoffman[9] state that this increase of pituitary hormone in the blood of women with ovarian deficiency is often evident in their urine, accounting for a certain percentage of the Aschheim-Zondek false positive results. This would very apparently be true, regardless of the test animal used. The other explanation is that a certain number of women who are several days late in their menstruation are in reality pregnant but miscarry so early that there are no gross evidences of the fact. This theory can further be substantiated when we consider that we obtained eight negative tests in women who were also three to five days late. None of these was pregnant.

There is another factor to be considered in any test that depends on the spilling over into the urine of a substance found in the blood stream, namely, the renal threshold value which we know varies with individuals and is not constant from day to day in the same person, as for example, sugar.[10] It appears that by analogy we should expect to find variation in the threshold value for the anterior pituitary hormone upon which this test is based. If this be true then it would also explain the 5 false negative results in 4 women.

CONCLUSIONS

The Freidman modification of the Aschheim-Zondek test for pregnancy offers the clinician a rapid and valuable aid in the differential diagnosis of pregnancy.

More research is necessary before the exact degree of reliability of the test can be definitely established.

The test will probably be of most value (1) as an aid in the diagnosis of ectopic gestation and (2) in uterine pregnancies which are inimicable to the welfare of the women, provided it is utilized as a laboratory aid to the clinical sense of the physician.

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DISCUSSION (*Abstract*)

Dr. Herman W. Johnson, Houston, Tex.—I have found this test a very valuable aid in the diagnosis of cases such as Dr. Kincaid mentioned, of ectopic pregnancy, and pregnancies complicated by pelvic tumors. It probably has a greater value to the surgeon than to the obstetrician, because the man who daily examines women suspected of pregnancy gains a greater degree of efficiency in diagnosis than the man who occasionally examines one. Of late years the general surgeon has been more inclined to refer cases of pelvic tumor to the obstetrician for examination for pregnancy, so the test comes to us at a time when the surgeon is protecting himself against meeting this complication. It seems to me a very valuable aid to the man doing pelvic surgery.

Dr. Hilliard E. Miller, New Orleans, La.—Obstetricians have searched for laboratory tests for pregnancy for many years. Tests such as the Abderhalden and glucose have not proven to be of any definite value. It was only after thorough experimental work and investigation of the actions of the endocrines in pregnancy that we were able to glean some definite facts about the hormones in the circulation and in the urine of pregnant women. The first observations of the behavior of the pituitary gland in pregnancy were made in 1904 by two French observers, who drew definite conclusions in regard to the physiological enlargement of the hypophysis during pregnancy. Evans, at a later date, determined that the injection of the extract of the pituitary body in the immature mouse produced definite maturation of the follicles of the ovary. This same observer showed that the transplantation of pituitary gland substance into immature rats caused the vagina to open, while a similar experiment on spayed rats would not cause the vagina to open, and the uterus showed only the atrophic changes which follow removal of the ovaries. It was also shown that the removal of the hypophysis caused a complete cessation of follicle formation in the matured rat, and the transplanting of the pituitary gland in these cases could cause a resumption of follicle formation, indicating that the pituitary gland was the activator of all follicle formation. An analysis of 258 Aschheim-Zondek tests by these two observers shows an error of 1.6 per cent. Robinson collected 2,358 cases and found an error of 1.47 per cent.

Freidman has recently called attention to a number of factors which might influence false positive and negative reactions in his modification of the Aschheim-Zondek test. Among these are buying rabbits indiscriminately from the market and use of an insufficient amount of urine. This authority states that 4 c. c. twice a day for two days is necessary if we are to get the best results in the use of this procedure. To a certain extent the period of pregnancy influences the amount of hormone excreted through the kidneys. Freidman states that 1/16 c. c. of urine from a woman seven months pregnant will induce definite hemorrhagic areas in the ovaries. Possibly the greatest use to which the test will be applied is in the diagnosis of cases such as ovarian cyst, myoma of the uterus, some of which it is almost impossible to differentiate from pregnancy. I personally have been confronted at the operating table with myoma of the uterus which it was impossible to distinguish from pregnancy without resorting to hysterotomy. The test will also be of great value in cases of chorioepithelioma and hydatidiform mole.

After the uterus has been cleared, as far as possible, with a curette of a hydatidiform mole, a positive Aschheim-Zondek test would indicate that this growth was still present. I have at present a case of chorioepithelioma which has been operated upon with an apparent clinical cure. For sixteen months a negative test on this particular case gives me a feeling of security insofar as the prognosis of the case is concerned. Should there be any metastatic manifestation of chorioepithelioma the test would undoubtedly be positive.

Dr. B. T. Beasley, Atlanta, Ga.—The Aschheim-Zondek test has already passed the experimental stage as it applies to the diagnosis of pregnancy. The value of the test may be shown in the following ways: first, as a positive diagnosis in uncomplicated pregnancy. Second, as a differential aid in diagnosing conditions simulating pregnancy or pathological pregnancies such as myomas, tubal pregnancy and in the death of a fetus. Third, in diagnosing hydatidiform moles and chorioepithelioma. Fourth, as a guide in prognosis in metastatic chorioepithelioma. It has been shown that the test remains positive as long as metastatic lesions remain active and negative when these lesions regress.

In our series of 52 cases in the white section of Grady (Municipal) Hospital we had an accuracy of practically 100 per cent in diagnosing uncomplicated pregnancy and we were able positively to differentiate myomas of the uterus from pregnancy, and prove the diagnosis at operation. We diagnosed two cases of hydatidiform mole, one case in which the mole had passed three weeks before and the woman had been curetted. She was later hysterectomized for severe hemorrhage and diagnosed as having chorioepithelioma.

It is possible that the reason why Dr. Kincaid had many reactions which he interpreted as negative was his method of interpretation of the reaction. Aschheim and Zondek have classified the reactions as I, II, and III. Reaction I is characterized by the maturing of the follicles, ovulation and estrum, and may be present in carcinoma or fibroid of the uterus. Reaction II is characterized by massive hemorrhages in the enlarged follicles and enlarged and hyperemic ovaries, tubes and blood vessels; and reaction III by the formation of atretic corpora lutea. The last two are positive for pregnancy and hydatidiform mole. If we interpret as positive only those having corpora hemorrhagica our degree of accuracy will be reduced considerably. According to the reports, the appearance of corpora lutea is just as positive as the appearance of corpora hemorrhagica.

Dr. R. A. Ross, Durham, N. C.—We began using the original Aschheim-Zondek test when it was first described. Later we followed Freidman's technic with the rabbit for the following reasons: it gave the same percentage of accuracy; it did not take as long; it

was easier to interpret; not as many anima's were lost; and it was cheaper.

Our false negatives all occurred in ectopic pregnancies, but at operation no living placental tissue was found. The hemorrhage had dislodged the fetal product.

We tried the test on two cases of teratoma of the testicle in the male. Both were negative, but both had received x-ray treatment before the test.

We have found the test of greatest benefit in the diagnosis of a woman recently delivered who has not yet begun to menstruate.

Dr. Arthur G. King, New Orleans, La.—May I call attention to the very recent publication of Wilson and Corner in the *American Journal of Obstetrics and Gynecology*. Their technic, which I had the privilege of studying, consisted of a single injection of urine, usually at five in the evening, in a mature, previously isolated rabbit. At nine the next morning the rabbit was laparotomized and the test read. The advantage of this regimen lay in the matter of speed and convenience, so that if an operation were indicated it might be performed that morning, within twenty-four hours of the patient's admission to the hospital.

In the matter of false positives, Dr. Corner always stressed the point that only a hemorrhagic follicle presenting the orifice of rupture of the ovum could be considered a positive. It must not be confused with the simple mature unruptured follicles or with a small dark-brown type of tumor on the ovary the explanation of which is not clear.

A real false positive can occur, rarely, to be sure. For example, it is known that experimental castration of animals results in an hypertrophy of the pituitary gland, and it is not unlikely that some forms of ovarian disorder may give the same phenomenon. We know that genital neoplasms have given false positives with the original Aschheim-Zondek test.

Corner and Wilson used the test not only for diagnosing early pregnancy, for studying chorioepithelioma, for distinguishing between ectopic pregnancy and the conditions with which it may be confused, but for determining the life or death of the products of conception. They found that a positive test disappears within 72 hours of the separation from the blood stream of live placental tissue.

We have used the test here in a few cases, many of them doubtful clinically, and the results have all been verified by subsequent events.

Dr. E. P. Allen, Oklahoma City, Okla.—I believe there is a possibility that this test will be of value in the toxemias of pregnancy, especially in the early cases of pernicious vomiting. We have had one or two instances where the reaction was so severe that the rabbit died very soon after the third injection. Whether this is due to the marked concentration of the urine or whether the toxemia has something to do with it remains to be proven.

Dr. M. Y. Dabney, Birmingham, Ala.—Any of you who were at the meeting of the American Medical Association in Philadelphia last spring I am sure will remember the excellent symposium that was presented on this subject. False positives and false negatives occupied a considerable part of the discussion. In my limited experience with the Freidman test I have tried to adopt some of these suggestions in the hope of eliminating some of the errors.

One suggestion is that before the test is done on the rabbit it is well to do a laparotomy to ascertain what the ovaries look like. In that case you will see the so-called false positive to start with. A false positive, as someone has described, is a sort of brown follicle; it has not the purple, coppery appearance that you get in a positive in a rabbit that has dropped a litter.

The question of anesthesia comes up. I think most men are using sodium amytal intravenously. Personally, I had quite a mortality at first, because on opening the rabbits 48 hours afterwards there is a certain amount of sodium amytal that has not been eliminated and the second dose often knocked the rabbits out. So now for the second anesthetic I give ether.

Another point brought out was that some observers said you do not always get a positive even if the patient is pregnant. I have seen that, and in one case that I reinjected 24 hours later I was surprised to find a definite positive.

The technic is to give 2.5 c. c. of urine or other material per pound into the blood. A four-pound rabbit would get 10 c. c. In 24 hours another 10 c. c., and in 48 hours we open the rabbit for laparotomy to observe the condition of the ovaries.

In ectopics most writers will admit you do not always get a positive result. About 25 per cent of cases are negative. I think we must remember that we do not necessarily get a positive in ectopic pregnancy.

Mature rabbits are much better than immature. Those that have had a litter are better.

There is a sociological side that is well to bear in mind. You say what is the use of diagnosing early pregnancy when you can be sure of finding out later. That is true, but the woman trying abortion when she has missed a period or two can be told whether she is pregnant or not, and only pregnant women will be subjected to the hazards of abortion.

Dr. Kincaid (closing).—I am thoroughly aware of the three reactions of the Aschheim-Zondek test: they were taken into consideration in the reading of these tests, but in order not to lengthen the paper unduly, they were omitted. The corpora lutea reaction was present in a number of instances, but seemed to predominate in the few tests which were done on women near term.

We had a number of false positives which had a dark-brownish appearance and which are very disconcerting in some instances. In those cases where they predominated the test was repeated.

False negative tests can be explained only on the basis that the rabbits were not sensitive to the anterior pituitary hormone, or that these particular women did not excrete in the urine the hormone upon which this test is based.

The rabbits were checked very carefully, only mature ones being used. As a minimum, 20 c. c. of urine were injected and at least forty hours elapsed before the rabbits were read.

In reference to the vomiting of pregnancy, the increased amount of hormone can be explained on the basis that the woman is excreting less urine and consequently it is more concentrated.

The ideal method of doing this test would be to examine the ovaries under anesthesia, thereby conserving the rabbit and helping to eliminate false reactions, but

this requires considerable outlay which the average man in practice would find almost prohibitive.

It seems to me that there is a tendency to explain away results that do not coincide with the clinical findings. I know of no laboratory procedure that will give perfect results when checked with clinical findings. I still feel that this test can be made of great value, provided it is used as an aid.

I did not discuss the value of this test in hydatidiform mole or chorioepithelioma because of lack of experience with this condition. It should be of considerable value when such a condition is suspected.

THE USE OF THE RABBIT IN THE ASCHHEIM-ZONDEK TEST FOR PREGNANCY*

By MARTHA A. WOOD, M.D.,
Houston, Tex.

Our first use of the Aschheim-Zondek test for pregnancy was in February, 1931. Since that time we have tried the test 102 times, using the rabbit as the index animal.

In the first 65 tests, 7 c. c. of early morning urine were injected directly into the left ventricle and the ovaries were inspected on the next day. As controls, many known negative and known positive cases were run along with the cases of suspected pregnancy.

Reinhart's article in the *Journal of the American Medical Association* recommending reinoculation with the urine if the ovaries were found negative after 24 hours, and a second inspection 48 hours after the first inoculation, caused us to adopt his reinoculation method with a few additions.

Our patient is asked to limit the intake of fluids after the evening meal and save the early morning urine, and to include the three or four o'clock morning urine, if she has the habit of passing urine at that time. The specimen is kept cold until it can be brought to the laboratory. About four ounces of urine are requested.

The specific gravity of the urine is taken, and the total amount passed at the time the specimen was saved is noted. (One of our patients brought in 750 c. c. of urine.)

The rabbits should be at least four months old and kept separate from the males.

As a control measure, the rabbit is anesthetized, the abdomen opened, and the ovaries are inspected. If the ovaries show no hemorrhagic follicles, but do show some small follicles on the surface, we consider the rabbit in condition for the test. The urine is filtered, warmed to body temperature and 10 c. c. of it are injected into the vein of the ear. About 24 hours later the abdomen is reopened, and if the ovaries show no marked change, another 10 c. c. of the same urine preserved in the ice box is injected into the vein of the ear. About 48 hours after the first inoculation of urine the third and final inspection of the ovaries is made, and the test is then reported.

The rabbit's abdominal wall is sewed up in two layers and the animal is kept for further experimental work. We have used some of our rabbits with negative tests several times, thus lessening the expense of the test. The smaller breeds of rabbits, such as the little Dutch and black Flemish, are more economical, both from the standpoint of amount of ether needed to anesthetize and the lesser food consumption.

We attach much importance to the preliminary inspection of the ovaries, as we feel that this gives us an ideal opportunity for correctly interpreting the actual changes brought about by the anterior pituitary hormone present in the urine. This procedure is, in our judgment, the best possible control of the test.

ANALYSIS OF 102 TESTS

Five tests lack confirmation, as it was impossible to trace the patients. Four patients have been under observation too short a time for a definite diagnosis to be made. Ruling these out in estimating our percentage of agreement of the test findings with the conditions present, we have 93 tests, 89 of which checked 100 per cent with the subsequent history.

Two cases of pregnancy gave negative results in the first two tests, the third test being positive. These four tests were done during the period when we were making only one inoculation. Our later experience with reinoculation as advised by Reinhart makes us feel that reinoculation would have probably given us a positive test at once in each of these two cases.

Since our adoption of the reinoculation method we have done 33 tests, 22 of which were negative, and the remainder positive. Of the 11 positive cases, I showed a positive reaction only after reinoculation and 48 hour inspection of the ovaries.

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*Read in Section on Pathology, Southern Medical Association, Twenty-Fifth Annual Meeting, New Orleans, Louisiana, November 18-20, 1931.

The other six positive cases showed very slight hemorrhages into the follicles 21 hours after the first inoculation. Reinoculation caused very prominent hemorrhagic follicles to show up at the 48-hour inspection.

No false positives have occurred in our series. The earliest positive test was 11 days.

The series includes: one negative test three days after a portion of retained placenta was passed. Laparotomy and curettage one week later showed miscarriage was complete at the time of the test.

One negative test, 48 hours after delivery of an eight-month old baby.

One negative test in a case of tubal abortion. Operation four days later showed that the area in the tube where the fetus had been implanted contained no fetal tissue. Much clotted blood was found in the abdomen. (See microscopic sections of the Fallopian tubes in exhibit.)

One negative test in a case of degenerated intramural fibroid. Hysterectomy was done a few days later.

One positive test in a suspected extrauterine pregnancy, which operation showed to be an ovarian cyst, with a two months pregnant uterus.

Three positive tests in cases where the question to be decided was whether a fibroid or pregnancy with some menstrual flow was the condition. Pregnancies were proven in all three cases. One of the cases, a negress, had both fibroids and a pregnancy.

In summing up the results of our experience with the Aschheim-Zondek test, we find it has proven very satisfactory. Our average percentage of agreement in the 93 cases carefully followed up was 96, with 100 per cent agreement in the 33 cases where reinoculation was done according to Reinhart's method.

DISCUSSION (*Abstract*)

Dr. J. A. McIntosh, Memphis, Tenn.—I wish to ask Dr. Wood how much we should charge for this test.

Dr. Seaborn J. Lewis, Beaumont, Tex.—This test is one of the greatest diagnostic discoveries in recent years. The reaction is 95 to 98 per cent accurate in the hands of the experienced worker, and that is more than we can say for the Wassermann reaction. I have had about 40 or 50 cases, and so far there has been only one doubtful result. It is necessary to have a good supply of rabbits of proper age and virginity, and preferably of the same breed. I prefer them to be at least fourteen weeks old.

This test, undoubtedly, will serve to prevent some useless and dangerous operations.

I have found it very easy to inject a marginal ear vein of the rabbit without an anesthetic. It is useless to try forcible restraint of the rabbit, as the animal will only struggle harder; instead, if an assistant will scratch the rabbit rhythmically between the ears, or just above the eyes, it will, as a rule, remain perfectly still while the injection is being made. I inject about 8 to 10 c. c. of the morning specimen of urine, preferably catheterized, and then autopsy the rabbit in about 36 hours. In an emergency, one may inject two or three rabbits, and autopsy one at the end of 12, 24 and 36 hours, but usually there is no urgency for the result, and the reaction is much more definite at the end of 36 to 40 hours. We must learn to disregard the doubtful reactions and to repeat the test in such cases. I prefer to examine the rabbit, under an anesthetic, before he expires, as the reaction is easier of interpretation while the blood is still circulating.

Dr. Harry C. Schmeisser, Memphis, Tenn.—The Aschheim-Zondek test for pregnancy impresses me as a remarkable contribution to the science of medicine.

It is based upon a sound physiological principle and should detect the presence of trophoblastic cells if they are present anywhere in the body, female or male. It should be of value not only in establishing an early uterine pregnancy, but also an ectopic pregnancy in the tube, ovary and abdomen, in a uterine hydatidiform mole, also uterine, tubal, ovarian, abdominal and metastatic chorionepithelioma. In the male it should assist in diagnosing the presence of chorionepithelioma which may occur in a teratomatous tumor of the testicle.

I wish to correct a statement just made by Dr. McIntosh that as far as he knew Dr. Reinberger was the only man doing this test in Memphis. Drs. Reinberger and Schreier, of the University of Tennessee, Department of Obstetrics, have both for some time been doing the test in their private practice. Since the early part of July it has been done at our Pathological Institute for the Memphis General Hospital by Drs. Dulaney and West. The Institute averages about ten tests per month. I am not prepared to tell you of their technic or results.

My introduction to the test was unexpected and somewhat dramatic. On July 9 a medico-legal case of rape was admitted to the Memphis General Hospital and the performance of the test was requested of our Institute. From the literature one received the impression that the technic was rather laborious, but as done for our Staff by Dr. Schreier it proved very simple. Two young virgin rabbits were selected. Into the ear vein of the first, a few c. c. of freshly voided urine from the patient were injected. Into the ear vein of the second, a similar amount of freshly voided urine from a known non-pregnant woman was injected. Twenty-four hours later both animals were anesthetized and their abdomens opened and the ovaries examined. Both ovaries of the control were normal. Those of the other rabbit both showed a typical positive test.

Dr. M. Jay Flipse, Miami, Fla.—My experience in this test is limited to a few cases seen in the routine laboratory work in our laboratory which we run in connection with the practice of internal medicine. In following the literature regarding the Aschheim-Zondek test we have found it difficult to select the simplest and most accurate of the various modifications described. In using whole urine we appeared to have a number of false negatives. More recently, therefore, we have been using Eberson's modification of the Aschheim-Zondek test, in

which the anterior pituitary hormone in 200 c. c. of urine is precipitated with alcohol and then washed with ether to remove the ovarian hormone, the resultant precipitate being dissolved in normal saline.

Our series of tests by Eberson's modification of the Aschheim-Zondek reaction has to date given us 100 per cent accuracy in proven positive and negative pregnancies. Eberson used white rats for his test animals. Occasionally we have used the same technic with rabbits, injecting the extract into the marginal ear vein. The results with rabbits appear to be as dependable as those on white rats, but it is somewhat cheaper to use rats and it is certainly considerably easier to raise rats than rabbits. Our usual charge for this test is $15.00.

Dr. May Owen, Fort Worth, Tex.—Until recently we have done the Aschheim-Zondek test simply as an aid in the diagnosis of pregnancy. Now we are doing some work on women who have been unable to carry their babies to full term, death occurring between the third and eighth month. In each instance, both the father and mother have had repeated examinations for conditions which might be responsible for the death of the fetus and the results have been consistently negative. Rabbits are injected with the urine every six to eight weeks from the beginning of pregnancy and the ovarian cysts compared with the previous findings. In one instance we have seen the cysts decrease in size and number until birth was given to a dead fetus.

Dr. C. R. Nelson, New Orleans, La.—How early do we get a positive test, and how long after a delivery? The earliest positive test that I have personally known was nineteen days after conception. Dr. Jeter, in Oklahoma, mentioned a patient who showed a positive reaction in four days.

We ought to try to secure reports of the earliest recorded cases, and of the duration of the reaction after childbirth.

Dr. G. H. Spurlock, Houston, Tex.—One of these patients was clinically pregnant. She had missed one period and the second period was almost due. She had the clinical evidences of pregnancy and I thought a slight enlargement of the uterus. I was sure we would get a positive reaction in this case. The other case I thought during the previous month had been pregnant. She went one week over her menstrual period, with the report that one week before that time she had passed a little mass. This time she went one week past her menstrual period and menstruated normally. At the time I furnished Dr. Wood the urine of this patient, she had gone two days over her menstrual period again and had complained of slight nausea. Dr. Wood reported a negative reaction, and I have a message from her this morning stating that she has menstruated.

Dr. Wood (closing).—In using the rabbit we felt that a charge of $10.00 was a fair fee for all concerned. About one hour's actual work covers the time for the test. Rabbits resist infection markedly, and strict asepsis does not seem to be necessary. Dr. S. J. Lewis taught me how to give an intravenous injection to rabbits. He runs the needle along the lumen of the vein for one-half inch or more, and holds the needle and ear beneath with one hand, giving the injection with the other hand, while an assistant strokes the rabbit's head to quiet it.

We feel that looking at the ovaries before injection is a most important thing, unless you can be very sure of your rabbits; and I do not know how you can be sure of them unless you take a great deal of trouble to keep rabbits on hand all the time.

All the cases that I have presented here have been observed over a period long enough for confirmation of the diagnosis.

Our earliest positive reaction was eleven days after conception. This was an illegitimate contact; and in this case the couple are now married. We have made only one post partum test. That was 48 hours after premature delivery, and the test was negative.

One ovary in one of our cases had no hemorrhagic follicles and the other ovary had some hemorrhagic follicles, so by all means examine both ovaries.

The question was asked whether it was proper to do the test for illegitimate cases which were not referred by a physician. The only two unmarried women whom I have treated were referred by physicians. In our laboratory we do other work for patients who are not referred by a physician, though we prefer, of course, to have the physician send them in.

Standardization of the technic is difficult at present.

TREATMENT OF CARCINOMA OF THE CERVIX*

By ROBERT H. LAFFERTY, M.D.,
and
C. C. PHILLIPS, M.D.,
Charlotte, N. C.

Since approximately 16 per cent of all cancers that we are called upon to treat are situated in the cervix uteri, it is important that we, as radiologists, keep this condition constantly in mind. It is vitally important that the general practitioner also be constantly reminded of this frequently occurring disease, and that the laity be informed in regard to the seriousness of the condition, and also in regard to its early symptoms.

We should all know the treatment that gives the best results and what may be expected from it.

We are presenting this paper for the purpose of adding this small series of compiled results to the literature.

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*Read in Section on Radiology, Southern Medical Association, Twenty-Fifth Annual Meeting, New Orleans, Louisiana, November 18-20, 1931.

It is not our purpose to discuss technic except to say that these cases were treated by the use of radium and x-ray and by radium, x-ray and surgery.

Total number of cases treated from 1922 to 1929	67
Number traced and analyzed in this report	60
Average age, years	50
Number 30 years of age or under (13 1/3 per cent)	8
Number between 30 and 40 years of age	7
Total number under 40 years of age (25 per cent)	15
Number giving no history of childbirth (Abortion in three months in one of these)	2
Average duration of symptoms before treatment, wks	38
Number operated upon after treatment (Three lived less than a year. Four lived 2, 3, 5, 8 years, 2 still living)	7
Early cases considered operable (One had hysterectomy following radium, one did not. Both living for more than 8 years)	2
Number who had postoperative recurrence before treatment (All died in a few months after treatment)	7

Only inoperable cases are analyzed in the following tabulation:

Number of inoperable cases	51
Number who lived less than one year	20
Lived from 1 to 2 years	10
Lived from 2 to 3 years (Still living 4)	8
Lived from 3 to 4 years (Still living 1)	1
Lived from 4 to 5 years (Still living 3)	5
Lived from 5 to 6 years (Still living 3)	3
Lived from 6 to 7 years (Still living 3)	3
Lived from 7 to 8 years (Still living 1)	1
Number treated prior to three years ago	39
Number of these 39 who lived more than 3 years (33 1/3 per cent)	13
Number treated prior to five years ago	30
Number of these 30 who lived more than 5 years (23 1/3 per cent)	7

CONCLUSION

There are two observations based on this report, to which we would call your special attention: (1) the relatively large number of young women who have carcinoma of the cervix; (2) the average duration of symptoms before treatment was instituted.

The only method for controlling either of these conditions lies in education: education both of the physician and of the lay people. The duty of disseminating this information and impressing it on those who only occasionally come in contact with this condition is incumbent upon those of us who are frequently called upon to treat these unfortunate sufferers.

DISCUSSION (*Abstract*)

Dr. J. W. Landham, Atlanta, Ga.—Drs. Lafferty and Phillips are to be congratulated that they have been able to follow up 60 out of a total of 67 cases treated from 1922 to 1929. Any follow-up system that works so well should be made generally known and I hope that the essayists in their closing discussion will tell us about it.

An analysis of the cases reported shows that the average age of this series of patients is fifty years, which places by far the most of the patients in the menopausal period. There are only two patients in the series who had not gone through childbirth. This emphasizes the fact that an unlacerated and uninfected cervix is rarely the site of a malignancy.

The essayists found 25 per cent of their group in women under the age of forty. I think this is unusually high and must be a pure coincidence. Certainly this has not been my experience.

The average duration of symptoms before treatment is thirty-eight weeks. This, of course, is a sad fact, but it simply means that an immense amount of educational work must yet be done among the laity.

Women approaching the menopausal age still think a discharge, intermenstrual "spotting," or hemorrhage is normal. Periodic pelvic examination should be done in all women approaching the menopausal age.

Martzloff classified carcinoma of the cervix into three groups: transitional, fat spindle cell, and the prickle cell type. He found that metastasis occurred during the first six months from the onset of symptoms in all types except the prickle cell type.

The number of clinical cures in this series certainly establishes the combination of roentgen and radium therapy as the best methods of treating all types of malignancies of the cervix regardless of the stage of the growth when the diagnosis is made. Any case of carcinoma of the cervix that can be cured by surgery can also be cured by radiotherapy and there is no mortality directly due to the use of radiotherapy.

Dr. J. M. Martin, Dallas, Tex.—I do not like the term "operable cancer of the cervix." I do not think any case should be operated upon at all, in view of the experience the better men are having with cases treated by radiation. In our community very few cases are being operated upon at all and these few are done by the class of surgeons who will operate upon anything, regardless of what it is.

In the early stages carcinoma of the cervix is curable by radiation, and in the later stages certainly all cases can be benefited. The Doctor said very little about the treatment of these cases. I shall mention one symptom which I think all cases have, certainly when the disease progresses far up enough to involve the ureter: that is, the great pain which these women have

in the ureter, which is due to hydronephrosis. That can be treated and relieved. The patients die from hydronephrosis rather than from cancer in our experience.

A doctor said this morning that the public knows more about cancer than the majority of physicians. That is probably so. The majority of physicians over the country have not kept up with the advance of knowledge of cancer.

Many of these cases will get well; others will be greatly benefited and their lives will be prolonged. Of course, when cancer reaches a certain stage, it is incurable by any means in the world.

Dr. Leon J. Menville, New Orleans, La.—The statistical study just presented by Dr. Phillips is certainly one of momentous importance, not alone to the radiologists who have experience in that particular field of medicine, but also to every practitioner of medicine. It should be given publicity.

Dr. Phillips has presented us with his results fol'owing radiation therapy and his message should convince the medical profession and the laity that radiation therapy judiciously applied by experienced radiologists is productive of great good.

Dr. Phillips (closing).—I fully agree with Dr. Martin about the "operable" and "inoperable" carcinoma of the cervix. I do not like the term "operable carcinoma of the cervix," either, and I wish I did not have to face so many of these cases that we must call inoperable. Nevertheless, it is a fact that we have to face the inoperable cases, and we cannot get away from that term. Neither do I think we can get away from the term "operable carcinoma of the cervix," because there are other branches of medicine practised besides radiology, and in some of these branches of medicine the term "operable" is quite acceptable.

The medical student should be given this information as he goes along through medical college, just as he is given information in all other lines. A number of these patients see a physician when these symptoms start, or when they cause annoyance or discomfort. They are then told that the symptoms are menopausal and will be corrected in a little while. A large number of patients have not seen a physician; and all the information a physician has is of no good to the public unless the public comes to see the physician. We have our national cancer control week in this country, which does some good, no doubt does a great deal of good; but when you present this subject to the people in a period covering one week no one person hears probably more than one talk covering twenty minutes, and this not more than once a year. It seems to me if the county medical societies could be interested in this condition and could get some representatives to meet with lay organizations all through the year, more discussion would be started among the laity and more interest aroused.

It is not a question of our extending ourselves and extending our branch of medicine in this, but, as I see it, of extending our service to suffering humanity, not for our own aggrandizement, but for what we may be able to accomplish in the relief of suffering.

CANCER OF THE ESOPHAGUS*

By PORTER STILES, M.D., F.A.C.S.,
Birmingham, Ala.

My excuse for presenting a paper on such an incurable and hopeless condition as cancer of the esophagus is the fact that hopelessness, as applied to a disease, should be considered as purely a relative term. Sooner or later death comes to all, and, merely because to some individuals we can predict with reasonable certainty that it will come soon, it does not follow that all of our efforts in their behalf are useless and a waste of time. If life can be prolonged, and a reasonable degree of usefulness and comfort be maintained, to do so is worthwhile. Perhaps the patient is engaged in the performance of some important work that he would like to complete; perhaps he has certain responsibilities which, if given time, he can place on other shoulders; or perhaps, to paraphrase "Ulysses," he merely feels that life piled on life were all too little, that death closes all, and, if to him but little remains, still every hour that is saved from that eternal silence is of value and a bringer of new things. Assuming, then, that it is but natural for one to cling to the life that he has, and feeling that it is our duty to assist in every way toward the consummation of that desire, I shall attempt to discuss briefly one of the saddest clinical pictures with which we are confronted.

Cancer of the esophagus, which term is used to include all of the malignant neoplasms of that organ, is more common than is generally supposed. Many cases are not recognized, and many of the recognized cases are not reported. In at least 5 per cent of the patients afflicted with cancer, the growth is in the esophagus. It has been noted by many observers that fully one-half of the esophageal lesions seen at esophagoscopy are malignant. Sarcomata and endotheliomata occasionally occur in the esophagus, but the great majority of malignant conditions of that structure are of epithelial origin. Differentiation usually can be made only by microscopic examination, as the history, symptoms, appearance and course are identical. The condition is much more common in men than in women, perhaps in a ratio of at least 5 to 1.

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Until more is known about the real cause of cancer, it is as useless to speculate as to the reason for this difference in susceptibility between the sexes as to attempt to explain the occurrence of cancer in anyone. As is the case with malignant disease in general, cancer of the esophagus usually occurs after the age of forty. However, some cases are seen at a much earlier age. I have had a fatal case in a man of twenty-three. The youth of the patient, therefore, should never be considered as sufficient evidence to discount the possibility of cancer.

Esophageal cancer may be primary or secondary. That is to say, it may be seen as a growth beginning in the esophagus itself, at the upper, middle or lower portion, or it may appear as a downward extension of cancer of the hypopharynx, an upward extension of cancer of the cardiac end of the stomach, or an extension into the esophageal wall from a growth in the mediastinum. Those primary in the esophagus may appear as ulcerating or fungoid growths, or as the scirrhous type with infiltration of the esophageal wall. Statistics as to the most frequent locations vary greatly in the published reports of different observers. However, it is perhaps universally found that endoesophageal growths are much more common than those that merely compress the esophageal wall from without.

In addition to its being a very important condition because of its frequency, cancer of the esophagus merits our serious interest because it is almost invariably fatal, this despite the fact that it usually grows slowly and gives rise to metastases very late in its course. No doubt many of us are prone to look upon this condition as being entirely hopeless from the start, and therefore to dismiss it as something beyond our power to control. It is true that we must await the announcement of some form of treatment for malignant disease as yet undiscovered before we can feel any assurance of uniform success in this field. However, we already have at our command the means of making an early diagnosis, and we have some methods of treatment which will prolong life, will make the final days more comfortable, and, in an occasional case, will actually effect a cure if we diagnose the presence of cancer sufficiently early to give the patient a reasonable chance.

Much has been written about the symptoms and signs of carcinoma of the esophagus. The literature has stressed the history of gradually increasing difficulty in swallowing food, of more dysphagia for solids than liquids, of pain in the chest and back, of regurgitation of food, the regurgitated material sometimes containing blood, and progressive loss of weight and cachexia. The blind passage of the diagnostic bougie often has been employed. Many suggestions have been made for differentiating spasm from cancer by the history, the symptoms, and the reaction to the bougie. Of course, any or all of the above symptoms can be present in cases of cancer, but they can be present in other conditions as well. In no sense of the word can they be considered as criteria for making an early diagnosis. It is well to remember that pain, though usually a prominent symptom of cancer elsewhere, is frequently absent in cancer of the esophagus, especially in the early stages. Marked loss of weight and cachexia, if due to cancer, are never early symptoms. The blind bougie can reveal little except the amount of obstruction and the tendency of the tissues to bleed.

The attempt to diagnose the presence and type of esophageal disease by clinical symptoms and blind bouginage is at best an inferential procedure and should have no place in modern medicine. We should employ as a routine the more certain methods of expert roentgen ray examination, followed by diagnostic esophagoscopy, with or without biopsy. Nor should we wait until the patient is having serious and continuous dysphagia before resorting to such examinations. We are now able with the fluoroscope and the use of proper contrast media, to study the outline and action of the esophagus during the act of swallowing and to record on the plate all of the abnormalities seen. We are also able to see and study in detail the appearance of the esophageal mucosa, and the condition of the esophageal wall and lumen, from the pharynx to the stomach, with the esophagoscope, all with practically no danger, and with very little discomfort to the patient. For this reason, every patient who complains of any unusual feeling in the region of the esophagus, or who presents any symptoms at all suggestive of dysfunction of that organ, should be subjected to direct examination without delay. The diagnosis of cardiospasm, globus hystericus or neurosis should never be made until fluoroscopic examination and diagnostic esophagoscopy have shown the absence of organic disease. It is only by employing this routine that cancer of the

esophagus can be discovered sufficiently early to encourage our efforts at cure.

The roentgen ray examination should be made first, not because the diagnosis might be made by that means alone, but because it will give information as to the presence of aneurysm and other mediastinal conditions about which the endoscopist should be informed. It should always be made by some one experienced in examinations of this type and competent to demonstrate and recognize small changes in the esophageal contour. The esophagoscopist should, of course, be sufficiently familiar with the appearance of the normal and diseased esophagus to be able to identify the changes that he sees and sufficiently certain of his diagnosis to justify his subsequent recommendations, however formidable they may be.

The esophagoscopic appearance of cancer varies with the stage and type of the growth and its location. In the early stages one may see only a small nodule or group of nodules. Sometimes the nodules are covered with eroded epithelium. In other cases the mucosa covering the nodules appears to be normal. More often one finds a well defined ulcer, fungoid in type, which bleeds easily. In other cases there is no ulcer, but the esophageal wall is found hard and thickened, a change that can be felt with the esophagoscope as well as seen. Blood may or may not be found with infiltrating lesions of this type. A small piece should be removed for biopsy in all cases where there is a fungoid ulcer or a papillomatous type of growth. Where there is nothing but infiltration, or apparently a compression of the esophageal wall from without, the removal of a specimen should not be attempted. It is entirely safe to remove a portion of any growth which projects into the lumen, or which can be reached without cutting through normal esophageal mucosa. In cases which show a bulging inward of the apparently normal esophageal wall, it is best to have the patient return after a month or two for further examination. To perforate the esophageal wall in an attempt to secure a specimen is to invite certain fatality from mediastinal infection.

Since we have good reason to believe that chronic irritation is often a precursor of cancer, the prophylaxis of cancer of the esophagus consists of removing or curing all forms of chronic irritation of that organ. That is to say, we should recognize and treat all non-malignant lesions of the esophagus such as foreign body, peptic ulcer, cicatricial stricture and cardiospasm. It is well, too, to advise against the use of very hot drinks and irritating foods.

Radical treatment must, at the present time, consist of surgical removal of the growth. The results of such efforts in the past have been most disappointing. There are many reasons for this. The approach to the mediastinal esophagus is technically quite difficult and the operation is very apt to be followed by serious shock and infection; there is no adjacent tubular structure that can be employed to replace an excised portion of the esophagus; and, because the esophagus has no serous coat, prompt healing without leakage of secretions can hardly be expected. However, with earlier recognition of cancer and with constantly improving technic, there is reason to believe that the future offers some promise of a larger number of cures. The radical operation is always a formidable and dangerous procedure, but we are dealing with a condition so hopeless that in some cases, and with the patient fully understanding the situation, such an extreme measure is justified. It is certain that the earlier we make the diagnosis, the more chance the surgeon will have for successful resection. It is equally certain that the earlier we make the diagnosis, the more successful will be our efforts at palliation when cure cannot be accomplished.

Palliative treatment is of two types, that directed toward controlling the growth, and that which has as its object the maintenance of the nutrition of the patient. The first type consists of the use of radium and the roentgen ray. The efficacy of these agents varies greatly in different cases. It also seems to vary according to the method of administration. In some cases radium itself can be applied directly to the growth. In other cases, the esophagoscopic implantation of radons is of value. In most clinics perhaps the best results are obtained by the skillful use of deep roentgen ray therapy, especially if it is started at an early stage. In the very late stages, when loss of weight is extreme and cachexia is well established, such treatment often makes the patient more toxic, shortens life, and is definitely contraindicated. Some cancers of the esophagus are much more radio-sensitive than others, for which reason uniform results are not obtained. For the same reason, deep therapy should be tried in every case, even if our results in previous cases have been disappointing.

For maintaining the nutrition, the quantity and type of the diet is most important. From the first it is necessary that the patient be sufficiently informed of his condition to secure his cooperation. The diet should be full and well balanced, but sufficiently liquid to pass through without causing irritation, stagnation or obstruction at the site of the growth. In addition to liquids such as milk and broth, pureed and strained vegetables and fruits should be given. Sooner or later, unless death occurs from infection, intercurrent disease or extension of the growth to other structures, the lumen of the esophagus will become too small to permit of proper feeding. Such being the case, it is wise to direct our efforts toward preserving the lumen at a very early stage. Gentle dilatation with the esophagoscope itself, or with the bougie passed through the esophagoscope, both procedures being under the direct guidance of the eye, are usually the safest and best methods at our command. In many cases, however, after esophagoscopy has disclosed the exact condition present, regular and gentle dilatation with the bougie alone can safely be employed. Rapid and forcible dilatation is sometimes resorted to, but even if the bougie is passed over a previously swallowed string, some fatalities from perforation or rupture of the esophagus are inevitable.

In the later stages of the disease, when a sufficiently large esophageal lumen cannot be secured and maintained by gentle methods, one must resort either to forcible dilatation or to gastrostomy. There is considerable difference of opinion as to which is the better thing to do. Both have advantages and disadvantages. Neither should be postponed too long, for if the patient is allowed to become dehydrated and almost starved before intervention is advised, neither will be successful. It is best, no doubt, to see that the patient thoroughly understands the situation and the outlook, and then to let him decide for himself which of the two alternatives he prefers. There is more danger of immediate death from forcible dilatation than from gastrostomy. Gastrostomy has the further advantage that, in addition to permitting adequate nutrition, it puts the esophagus at rest and prevents further irritation of the growth. However, to many patients, the thought of being forced to receive all of their food through a tube the rest of their life is intolerable, and, in such cases, gastrostomy is but an added misery to a dying man, and usually hastens death. There are others to whom the prolongation of life is the all-important thought and the method of nutrition of no consequence at all. For such patients gastrostomy, performed early, is the preferred form of palliative treatment, and should always be employed.

In conclusion, I would like to emphasize the fact that cancer of the esophagus is not a condition that should be treated by one man. The cooperative services of the internist, the surgeon, the endoscopist and the roentgenologist should be obtained for every case. Early diagnosis is most important, and then, unless radical removal is to be attempted, treatment for retarding the growth of the tumor and maintaining the nutrition of the patient should be instituted at once. We can offer these unfortunate patients very little hope of actual cure, but if started sufficiently early, our efforts usually can secure them many months and sometimes years of comfortable and useful life.

501 Medical Arts Building

THE TREATMENT OF THE POTENTIALLY INFECTED ABDOMINAL WOUND, AND ITS RELATIONSHIP TO THE MORTALITY OF ACUTE INFECTIONS OF THE ABDOMEN*

By H. A. GAMBLE, M.C., F.A.C.S.,
Greenville, Miss.

Wound infection has a greater influence upon the morbidity and mortality of acute intra-abdominal surgery than any other single factor. I am not referring to infections of supposedly clean wounds, as for instance stitch abscesses, but to those conditions in which we recognize gross contamination at the time of operation: such as cases of general peritonitis, appendical abscesses, gangrenous perforated appendices, gangrenous gall-bladder, perforated lesions of the hollow viscera, gunshot wounds of the abdomen, and intestinal obstructions.

It is a well established fact that the lower ileum and the cecum are the natural habitat of a number of anaerobic organisms, especially the bacillus of Welch. Williams,[1] in an article upon the toxemias of intestinal obstruction, states that the bacillus of Welch is an organism which requires for its growth and the production of a

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toxin an anaerobic medium which should be neutral or slightly alkaline, and that the lower ileum is the only part of the gastro-intestinal tract which fulfills these conditions. The acid condition of the stomach above and the colon below restricts the growth of the bacillus to this region.

In this country, Jennings[2] has done a great deal of work in regard to the relation of *Bacillus welchii* to appendicitis and its complications. He states that Welch's bacillus is present in most appendices and is frequently found outside the gut actively growing in appendicular abscesses, in localized peritonitis, and in a rather large number of cases of free peritoneal exudate. In most cases its activity is cut short by operation and the removal of the appendix, but this is not always the case, and *B. welchii* is apparently an active factor, if not the most active factor, in the production of a fatal outcome.

Clinically it has been our experience that the bacillus of Welch is not confined to appendicitis and its complications. It may be found in any acute abdominal inflammation. Two of the eight cases of fulminating gangrene of the abdominal wall reported by us were associated with an acute intestinal obstruction, two with acute cholecystitis, one with chronic cholecystitis, three with either gangrenous appendices or appendical abscess, besides which we have frequently seen in wounds associated with these diseases a localized gangrenous process which no doubt was due to the same organism.

Because these anaerobic organisms are present in a large proportion of acute intra-abdominal lesions, I feel that we are fully justified in considering all such wounds definitely infected at the time of operation. The course of the infection is influenced by the individual's resistance, the virulence of the infective organism, and the presence of other organisms, but most of all by the method of treatment.

These wounds can be placed in two categories: first, that in which the infection remains localized, and there is only local death and sloughing of wound tissues; and second, that in which there is a fulminating type of infection gangrenous in character, which spreads between the fascia of the abdominal wall and the subcutaneous fat, or sometimes in the intermuscular planes. There appears to be a general opinion that these fulminating lesions are rare. We cannot believe that our experience is unique, but feel that at the outset the symptoms are more constitutional than local, and because they are of a toxemic character and occur on the heels of an abdominal catastrophe, one is liable to ascribe them to the original disease rather than to a secondary complication.

In the literature for the past twenty years there is an extreme paucity of reports upon these wound infections, and no suggestion as to prophylaxis.

Bier[3] reports one case following an appendical abscess, with ultimate recovery, and states that it is surprising in view of the fact that the intestines are the habitat of many anaerobes, that more cases of spreading gangrene of the abdominal wall are not seen.

The late A. J. Ochsner[4] reports a case, with the following introductory remarks:

"The gas bacillus infection following operations for gangrenous appendices is so rare and the outcome so commonly fatal that it seems worth while to report this case which recovered."

Butler[5] reports two cases, one following operation for perforated appendix which recovered, and one following operation for acute intestinal obstruction which died. Butler and Rhodes[6] report one case. Horsley[7] reports a case of gangrene of the abdominal wall which would be properly classed as this type of infection. Shearer[8] reports a fatal case with the remark that gas gangrene of the abdominal wall is an extremely rare and serious condition. Several cases of slowly spreading gangrene of the skin have been reported. This, however, is an entirely different entity from the condition under discussion.

The three cases of my own which were first reported at the Mississippi State Medical Association in 1925, and abstracted in the volume on "Surgery" of the "Practical Medicine Series," 1926, with the five cases following make eight cases that I have personally treated during the past seven years.

Case 1.—E. F., a white man, age 42, a drug addict, suffering from recurrent attacks of gallstone colic, was operated upon October 18, 1926, the appendix and gallbladder both being removed. Three days following operation the patient had a temperature of 102°, pulse 110, and the wound was swollen. The wound was opened, the tissues were found to be edematous and yellowish green in color next to the fascia. This discoloration was followed outward by an incision extending to within four inches of the midline in the back. The condition continued to spread, however, until it involved practically the whole of the abdominal wall, and the patient died on November 11.

Case 2.—T. J. S., age 52, a white man, was admitted September 24, 1927, and operated upon the same day for an acute intestinal obstruction of twenty-four hours' duration. The obstruction was found to be due to a band of adhesions about one-fourth inch in width, which was released. An enterostomy tube was placed in the proximal end of the gut and brought out through a stab wound in the left side of the abdomen. The abdomen was closed without drainage except for prophylactic strips of rubber between the stitches in the skin. This

patient developed a gangrenous infection in the wound, and on September 28, his temperature being up, the stitches were removed from the wound, with the escape of sanguinolent fluid and some gas. The wound was gangrenous and the infection had spread subcutaneously toward the left side of the abdomen. The patient died October 5 from suppression of urine, the gangrenous process having never been controlled.

Case 3.—J. N. R., age 22, a white man, was admitted July 29, 1930, with a diagnosis of acute gangrenous appendicitis. He was operated upon immediately, and the operative record shows that one large penrose drain was placed down to the stump of the appendix, the peritoneum was sutured and two sutures were introduced into the internal oblique and transversalis muscle. The remainder of the wound was packed with gauze soaked in 2 per cent solution of mercurochrome after being flushed with ether. The patient's condition at first was apparently very good. On August ' he complained of a great deal of discomfort. His temperature was normal and pulse 80. On August 3, however, his temperature went up to 104°. The sutures were removed from the internal oblique muscle and a gangrenous area was exposed. His fever continuing high on August 4, while no definite areas of infection could be elicited, an incision was made posteriorly two inches from the costo-vertebral angle and gangrenous tissue was encountered beneath the transversalis muscle. This wound was extended forward until it united with the original appendical wound, and it was packed with gauze. As soon as oozing had stopped the gauze was removed and the wound left open to the air under a frame or coop. From this time on, the patient had an uninterrupted convalescence.

Prior to this case, in all cases that had come under my observation the infection had spread between the fascia and the subcutaneous fat of the abdominal wall. In this instance, however, it evidently spread between the peritoneum and transversalis muscle.

Case 4.—W. H. S., age 49, a white man, was admitted to the hospital November 17, 1930, suffering from acute appendicitis. The appendix was removed, one penrose tube inserted down to the stump, and the abdominal wall closed in layers down to the tube. On November 20, the patient developed symptoms of postoperative intestinal obstruction, and an enterostomy was done on the left side of the abdomen, the enterostomy tube being brought out through a stab wound. The opening in the abdomen was closed with one penrose drain. The patient had a rather stormy time with a temperature ranging from 101 to 102°, and on November 29 the wound following the enterostomy was opened to its depths and found to be gangrenous. It was enlarged and all gangrenous areas were exposed to the air. He was discharged from the hospital January 11, cured. The number of days in the hospital was 55.

Case 5.—F. G., age 70, a white man, was admitted to the hospital June 6, 1931, with a temperature of 105° and a history of having been sick for three days. A diagnosis of acute cholecystitis was made and the gallbladder drained and stones removed that same afternoon. The wound was closed except for rubber drains between the stitches up to the cholecystostomy tube. The patient's temperature dropped to normal within a few hours. However, twenty-four hours later he began to develop a jaundice, showed some mental wandering and his pulse went up to 130. The wound was opened, and bubbles of gas were seen escaping from it, with gangrenous tissue throughout. The infection rapidly spread outward despite the wide opening up of the infected areas and the use of anti-gangrene serum. The patient died on the fourth day.

SYMPTOMS

Local sloughing and abscess formation is usually preceded by some elevation of temperature, leucocytosis and pain in the region of the wound, the cause being easily determined upon removal of a stitch.

In the fulminating type of infection the early symptoms are almost entirely constitutional in character. They are slight icterus, fever, increased pulse rate, high blood count, and hiccoughs, with but little evidence of any local complication, so that, as was said previously, one is liable wrongly to ascribe the symptoms to the original peritonitis which it even simulates in many respects. However, if one will keep in mind the fact that the peritoneum is wonderfully capable of overcoming infection and appears to have a special immunity as regards the bacillus of Welch, he will not be misled. Personally I have seen but two patients die of peritonitis, among over 1,100 cases of acute appendicitis treated since January, 1920, 415 of which were drainage cases. One hundred and fifty-four of these had a generalized peritonitis. The two were moribund when seen, one with a perforated appendicitis of four days' duration and one of five days, and neither of these patients lived more than four hours.

With symptoms such as those just enumerated following an operation upon an acute abdomen, we feel no hesitancy about an exploration of the wound. The third case reported had been treated according to the technic to be described except that the internal oblique and transversalis muscle had been sutured with interrupted catgut. His symptoms, fever, rapid pulse, high blood count, hiccoughs and abdominal distention were suggestive of a peritonitis. It was assumed that the infection had spread outward in the intermuscular plane and an exploration was made posteriorly near the angle of the last rib, which showed the spreading gangrene between the peritoneum and the transversalis. This wound was prolonged forward to the original wound with immediate abatement of symptoms.

Treatment can and should be preventive. Once the fulminating type of infection develops, one has to open up all infected areas to provide

drainage and exposure to the air. Besides one should employ various measures to maintain the strength of the patient and to overcome the infection, namely: nourishment, fresh air, blood transfusion and glucose intravenously. We have employed anti-gangrene serum, but believe that it would prove more efficacious as a preventive than as a curative agent.

As a prophylactic measure we have adopted the following procedure in all potentially or grossly infected wounds. After dealing with the intra-abdominal lesion the peritoneum is sutured (a rubber Penrose drain if necessary being left at one angle). The wound is washed with ether, silkworm gut sutures are introduced down to the peritoneum and the wound is flushed with 1 per cent aqueous solution of mercurochrome and packed full of gauze saturated with the mercurochrome solution over which the silkworm gut is tied in a bow knot. The patient is placed in bed in whatever position will most favor drainage.

We have tried leaving the wound open, but believe that our present technic is preferable, first, because for the first seventy-two hours the strength of the abdominal wall is maintained, and secondly, we believe that the pack in the wound is not only antiseptic in its action, but from a physiological standpoint is conducive to a retrograde flow of the lymph until nature has been able to throw up her protective bulwarks.

The pack is changed every twenty-four hours and at the end of seventy-two or ninety-six hours all packing and dressings are discarded, the patient is placed bare under a coop and the wound left exposed to the air and the light from an electric bulb.

These wounds all heal kindly and quickly, and to our belief this is the most logical method of combating an anaerobic infection, at the same time eliminating pus poultices.

The proof of the pudding is in the eating. From January 1, 1920, to January 1, 1925, we treated 137 drainage cases of appendicitis by partial closure with two cases of fulminating gangrene and one case of gangrene from an acute cholecystitis in which the wound was partially closed. From January, 1925, to date there were 292 drainage cases, 141 of which were treated in this manner. Among these, there were 82 cases of general peritonitis, all of which were considered grossly infected, in which no case developed a severe wound infection.

The additional cases reported today developed in the 151 partially closed wounds seen since 1925. We feel that personally we have learned our lesson. Whenever we have tried to get away from basic surgical principles in the treatment of these manifestly infected wounds we have come to grief.

Nowhere else in the body would we consider closing an infected wound, particularly when the odds all are that it is also anaerobic in character. It is a violation of the most fundamental surgical principles.

These patients have had an unusually uncomplicated convalescence and I feel convinced that if the principles spoken of today are observed in the treatment of infected wounds, there will be a marked lowering in the mortality as well as in the death rate following acute abdominal catastrophes.

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MANAGEMENT OF THE ASTHMATIC: SOME POINTS OF GENERAL INFORMATION*

By B. G. EFRON, M.D.,
New Orleans, La.

Introduction.—Since the advent of allergy as a specialty in medicine, the treatment of asthma has undergone a radical change. Specific measures have replaced numerous and often futile procedures. However, many misconceptions are still prevalent concerning allergic methods. The management of the asthmatic must go back further than the care of the particular case. The physician in charge must be acquainted with the principles and practices in allergic disease. The prevalent fallacies in relation to allergy must first be corrected.

Allergy must be recognized as a pathological entity that has taken a firm place in medicine, and the idea that a few scratches will lead to a spectacular diagnosis and an almost miraculous cure must be abandoned. Another idea that should be scrapped is that nothing at all can benefit an asthmatic but a change of climate. Time and time again we see patients who have been told by physicians that their case is hopeless.

Patients very often say: "I have had the skin tests and they have not benefited me;" "I have taken the serum, but am no better." Often it is very difficult to convince these cases that perhaps the survey made on them was incomplete and that there is not one so-called "serum," but any number of antigens, and that perhaps the antigen used was not the correct one for their case.

The truth lies between these two extremes; many, if not most cases of asthma, are definitely benefited by the use of allergic methods, a few are cured, and some are not relieved at all. With most cases, observation over a long period of time is necessary; at times a year's observation of a case is required in order to evaluate all of the etiological factors.

History.—In allergic diagnosis the causal agents, and not the nature of the ailment, is desired. The patient usually knows only too well the nature of his trouble. There are a few exceptions, but we shall not discuss these at the present. The history is the most important single procedure in allergic diagnosis. It should be in the nature of a careful cross-examination. No question or fact can be disregarded; so much so that not even a patient's religion may be discounted. We traced a case of asthma to cheese, because the patient, a growing boy, had his attacks most frequently during week-ends. The child was a member of a devout Catholic family and the attention of the parents was called to the frequency of his attacks at week-ends by his inability to attend church regularly. The season during which asthma occurs is most important. Asthma occurring only in summer is usually caused by pollens; winter asthma is often caused by house dust.

The effect of environmental factors is important because often etiologic clues are disclosed by the patient. The patient who states that he or she cannot tolerate the sweeping of a room is sensitive to house dust. The woman who has attacks after a visit to the beauty parlor or after a dry shampoo, or after using perfume, is most likely sensitive to orris root. Attacks that come in the afternoon are very likely due to foods or unusual contact. When dyspepsia precedes attacks, foods should be suspected as the cause. Contacts with animals or pets by the patient or by relatives should be inquired into. Many attacks are caused by the danders of animals.

The effect of locality and change of locality is very important. A patient may have asthma in one house and not another. In such cases, a careful check-up of the environment in each house is important. House dust cases very frequently lose their asthma when transferred to a hospital. Pollen sensitive patients often are relieved by a change of climate; they are particularly well on the high seas and often much better at the seashore.

The patient's occupation is important. Asthma due to occupational dusts are not infrequent.

The effect of aspirins and other frequent medication should be investigated. Many cases are relieved by aspirin. On the other hand, aspirin may be responsible for many severe attacks.

Previous treatment should be recorded. The patient who has been on a diet eliminating fish, cheese, eggs, meat, and milk, and has not been relieved, is not sensitive to those foods.

The type of heat used in the patient's home is important. A hot air heating system is bad for cases sensitive to house dust.

The cleaning methods used in the patient's

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home should be investigated, as should be the kind of mattress, pillows and bedcovers that are used. Very often a visit to the patient's home may disclose a possible etiologic factor. Multiple sensitivity is the rule, so that the history can never be too minute or too painstaking.

Physical Examination.—The physical examination is usually of secondary importance. In most cases few etiologic factors are discovered. Foci of infection should be eliminated, but with conservatism as a keynote. The foci should be eliminated perhaps a little more readily than if there were no asthma present, but by no means with the enthusiastic expectation that the asthma will cease when they are removed. Nasal and throat surgery should not be undertaken during the patient's pollen season.

Skin Tests.—There is much misunderstanding concerning the value of the skin tests, varying from the fond expectation that a few scratches into which some allergens are rubbed will yield an etiologic diagnosis, to the ultra pessimistic view that they are of no value whatsoever. The skin tests, whether dermal or intradermal, when properly made, and by that I mean:

(1) When a sufficient number of allergens pertaining to a case, as indicated by the history, are used.

(2) When the tests are done correctly, and

(3) When the reactions, both immediate and delayed, are compared with a control.

and the tests properly interpreted, that is, interpreted in the light of the history, are a valuable adjunct in arriving at a diagnosis. The skin tests should be regarded as a step in the investigation and not the end of the search. Retesting may be, and often is, necessary. When the results of testing do not fit the history, these may be ignored. Thus, a winter asthmatic giving a reaction to Bermuda grass does not have his winter attacks because of pollinating Bermuda. At times positive reactions are not indicative of the cause of the trouble, and sometimes known allergenic substances give negative reactions. The skin tests should be considered the beginning and not the end of observation.

Treatment.—The treatment should be based on the findings in the history, physical examination and the skin tests. The epidermal dust and pollen cases should be treated by avoidance and desensitization. The food cases should be treated by avoidance. Only in unusual instances should desensitization be tried with food allergens.

In perennial cases, different antigens, given in seriatum may be required. During hypo-sensitization treatment the reaction obtained following any injection is the criterion for further increase. The dose should not be increased if any injection is followed by a large local reaction of redness, heat or swelling that lasts 24 hours or longer. In such a case the dose should be repeated till the local effects are slight or absent. If any injection is followed by an attack of hay-fever, asthma, hives or nettle rash, this reaction should be controlled by injections of 0.5 to 1 c. c. of suprarenalin until relief is obtained. The next dose should be one-half the dose which caused the reaction. Particular care should be exercised when changing from an old to a new antigen, and when changing from a weaker to a more concentrated dilution.

When diets arranged according to the reactions obtained by skin tests fail to give the expected relief, the elimination diets of Rowe may be tried. They are quite useful, and often by means of them, allergens are discovered that the skin tests fail to incriminate.

The control of the actual attack is of such importance that it is necessary to mention it. Adrenalin is the drug of primary importance. It will cut short an attack if given in large enough doses hypodermically. Doses may be repeated as often as 15 minutes apart. It is absolutely inert when used by mouth or when held under the tongue. Ephedrine, *per orem*, is valuable only during mild attacks. A few patients cannot take it because of the uncomfortable sensations it causes, such as nervousness and vertigo. Tolerance to ephedrine is often acquired in a very short time, however. Morphine may be used at times. Many patients have found various measures that will help them; they should be encouraged to use them. Some find whiskey and aspirin beneficial, others black coffee, and various other measures.

CONCLUSION

In conclusion, the management of the asthmatic requires careful watching and study. Treatment must be based upon the etiologic factors responsible. The etiologic factors must be discovered by means of the history, laboratory tests and clinical trial.

SYMPOSIUM ON MALARIA, Part 1*

PROBLEMS IN MALARIA IN HAITI*

By S. S. Cook, M.D.,†
Port-au-Prince, Haiti

In limiting my brief remarks to the problems of a very small part of the Tropics, I am fully aware that this is a departure from the usual tenor of a chairman's address. However, the situation in Haiti must parallel in many respects that of other independent republics throughout the hot countries of the world. For those of you who have not been so fortunate or perhaps unfortunate as to spend time in these countries, I hope to depict to you something of what malaria means to inhabitants of such places and also some of the disappointments and at times heart-breaking failures that fall to the lot of those who are attempting to improve health conditions for them.

Records left by the physicians of the French Colonial period indicate a high prevalence of malaria in Haiti during that period. Although the disease was not clearly distinguished from other diseases, notably yellow-fever, yet their description of fevers of tertian, double tertian and intermittent forms leave no doubt that malaria was an important factor in mortality and played a large part in hindering the development of the country. In 1801, Captain General LeClerc, brother-in-law of Napoleon, arrived in Haiti with an army of 25,000 men and a supporting navy. His orders were to conquer the country and reinslave the natives. Six weeks was regarded as ample time to accomplish this task. Within a year, and despite large replacements from France, his army had become decimated by yellow-fever and malaria. In November 1802, he died a victim of yellow-fever and malaria, thus ending one of the most complete defeats of an army by disease in all history.

The Island of Haiti is the second largest of the West Indian Islands and lies between Cuba and Porto Rico. Its location is between parallels 17° 39′ and 20° north latitude and between meridians 68° 20′ and 74° 30′ west longitude. The rough horseshoe shape of the Republic of Haiti gives it quite a disproportionate amount of coast line as compared with its area. With its island dependencies it has about 1,000 miles of coast, while its total area is only 10,000 square miles. Likened to a piece of paper crumpled in the hand, the Republic is made up of one series after another of steep mountain ranges, the general direction of which is from east to west. Between the mountains there are wedge-shaped valleys and plains. The total area of all of the plains of importance probably does not exceed 2,000 square miles or one-fifth of the area of the Republic. It is characteristic of the plains in general that they require irrigation to obtain reliable crops. In some cases this is due to insufficient annual rainfall and in others to an unsuitable distribution throughout the year.

In general, the drainage of Haiti is by small, swift mountain streams. One of the characteristics of these streams is that they lose much of their water through crevices in the limestone or underlying strata of large gravel before reaching the sea. Some fair size streams disappear entirely during a large part of the year. This characteristic accounts also for the sluggish and intermittent character of some of them in their lower portions and for the occurrence of large numbers of pools and backwashes which are filled with flood water, but remain undisturbed between floods. These pools are often sources of abundant breeding of anopheles mosquitoes.

The temperature in Haiti is notable for its remarkable equability. For any given point the range between the maximum and minimum temperature is very small. Except for a few small settlements in the mountains, there is no place where the temperature goes below the minimum required for mosquito breeding. The rainfall is subject to great variations, both as regards locality and season. There is no uniform rainy season for the whole island. Within the past two years there have been unusually heavy and unseasonal rains in many parts of the island. In Cayes there has been considerable rainfall almost every month. Cape Haitian witnessed frequent heavy downpours in what is ordinarily the dry season. In and around Gonaives ponds, covering hundreds of acres, have been formed where there had been none for the previous 15 years. Rainy days, an uncommon occurrence in Haiti, have been observed throughout the island. Dry pasture land within the city limits of Port-au-Prince has been converted into a boggy seepage area.

There has been no census of population within the past century. Due to many difficulties it would be a highly expensive and almost impossible task. An estimate of 2,000,000 is more generally accepted than any other. There are nine cities with a total estimated population of about 200,000. Thus it is seen that 90 per cent of the population would be designated as rural.

All towns and villages are built on or near streams, which has a direct bearing on the incidence of malaria.

Agriculture on a small farm basis is the principal industry of the country. A sugar mill near Port-au-Prince, a pineapple cannery near Cape Haitian and a

*Chairman's Address, National Malaria Committee (Conference on Malaria), meeting conjointly with Southern Medical Association, Twenty-Fifth Annual Meeting, New Orleans, Louisiana, November 18-20, 1931.

*From the American Scientific Mission to Haiti.

†Lieutenant Commander, Medical Corps, United States Navy.

*Part 1 of a Symposium on Malaria, comprising principally papers and discussion before the National Malaria Committee. Part 2 will appear in the June issue of the Journal.

sisal plantation, also near Cape Haitian, comprise all of the major industrial developments.

The peasants, largely of African descent, live on or near their small farms. Their houses have mud walls, dirt floors and thatched roofs. Although all windows and doors are closed at night, space along the eaves and around the doors permits easy entrance of mosquitoes. Living as they do outdoors most of the day and into the night, screening, even if it were practicable, would be of little benefit. Their usual bedtime is shortly after dark and they commence the next day while it is still dark. People from the hills come down to the towns for market, often spending a part of the night en route. Those who live at altitudes where anopheles are not found are thus exposed to malaria. Another source of infection is the Saturday night dance or "bambosh," to which people may travel miles. These dances are held throughout the Republic and are attended by almost the entire population. Beginning at nightfall, they frequently last until after daybreak.

The oft-repeated statement that malaria, yaws and intestinal parasites are the chief diseases does not entirely cover the case. To these should be added malnutrition. In the examination of over 12,000 school children in Port-au-Prince note was made of those who showed gross evidence of malnutrition. The percentage varied from 10 in the high class private schools to as high as 54 in the poorest sections. Dental surveys indicate a very high incidence of dental caries, a large part of which is attributed to improper diet. Experience here indicates that among the natives the incidence of malaria or malarial paroxysms varies inversely as their nutrition. The countrymen and also the working class in the city have no regular meal hour. They eat when hungry, the meal consisting of whatever is available or what may be purchased with the amount of cash which happens to be at hand.

Over a million and a half illiterate, superstitious people living as did their primitive African ancestors, riddled with disease, down-trodden by those no less ignorant but far less honest, fighting wars of which they knew nothing, afraid to tell even their right names; such was the pitiable state of the Haitian peasant in 1915.

Since 1919, when the National Public Health Service was created by law, much has been accomplished. Ten modern hospitals have been built in accessible towns of the Republic. Free clinics are held in nearly 150 places, where all who apply are treated. No longer are the streets cluttered with beggars whose bodies, a mass of sores, were horrible sights to passersby. Gone, we hope forever, are epidemics of yellow-fever and smallpox. Greatly diminished are the horrible ravages of yaws whose lesions yield quickly to arsenicals, bismuth and mercury. But what of malaria? Progress has undoubtedly been made. Concentrating activities near centers of population, the usual anti-mosquito measures have been employed. Miles of ditches have been dug, street sweepings have been used to fill swampy areas, and much Paris green and oil have been applied. Quinine has been distributed through health centers, hospitals and rural clinics. Information has been propagated through available channels.

Despite strenuous efforts malaria remains an outstanding problem and a long-time challenge to the National Government. Can malaria be satisfactorily controlled in Haiti? Under existing economic, social and political conditions the answer must be in the negative. The solution is in some respects simple; in others, highly complicated and difficult.

Along with the rest of the world, Haiti has suffered severely in the past two years. The low price of coffee, her chief export, has been keenly felt. Haitian coffee has for many years been highly regarded in France. Coffee production in some of the French colonies of Africa bids fair to curtail in large measure this outlet. Haiti does not at the present moment produce a single commodity essential to world trade. Interesting possibilities for future development are: cotton, corn, tobacco, cattle raising and fruit growing, particularly pineapples and grape fruit.

Agricultural enterprises on a plantation basis could, if properly managed, materially assist in the campaign against malaria. Moving the laborers into well sanitated villages with ground for gardens would go a long way toward reducing the incidence of intestinal parasites and would also greatly improve the nutritional status of the people.

The educational system leaves much to be desired. In the towns and cities there are many good schools through which the teaching of hygiene and sanitation can be carried on. In the rural districts teaching is highly irregular. The teachers are poorly trained and poorly paid. Many years must elapse before the country schools can be looked to as distribution centers of health information.

With the available statistical data one is unable to say whether malaria is increasing or diminishing in the country as a whole. There are no doctors in the rural districts and very few in any of the towns except the ten district centers. In the public health hospitals the number of admissions and deaths due to malaria are known. This information is of slight statistical value, as the proportion of the population from which they came is unknown.

The successful control of malaria in Haiti, and the same conditions doubtless apply to many other countries, demands first of all an efficient and well managed health department free from political interference. Trained sanitary inspectors are scarce and the removal of one for political reasons often leaves no one capable of filling the position.

Funds for carrying on drainage and other sanitation projects are of course essential. To obtain them requires cooperation and perseverance. The availability of money depends on the economic status of the National treasury and is beyond the control of the Health Department. Securing of funds from the treasury requires that the Director of the Health Service present

a carefully prepared comprehensive program setting forth his needs in detail. To obtain the information on which to base such a program the Director must be fully cognizant of conditions throughout the Republic. Such information may be secured by frequent visits to various parts of the island and through detailed reports sent in by conscientious district public health officers.

Having fulfilled these requirements, it now becomes necessary to consider the plan of attack. Experience has definitely shown us that this disease must be approached from two angles, namely: the human carrier and the insect vector. Malaria surveys made by the Rockefeller Foundation, the United Fruit Company and the National Public Health Service have revealed the island-wide distribution of the disease, and have also shown its relative intensity. To treat all the carriers of malaria in Haiti is a task that staggers the imagination. Such an undertaking could not be accomplished through existing agencies. Even with unlimited funds for drugs and personnel the people have not been educated to the seriousness of the disease and would most certainly defeat the plan through lack of interest and ignorance. However, inability to secure complete success should not deter those in authority from putting forth every effort to alleviate conditions.

Surveys made by the Rockefeller Foundation and the National Public Health Service furnish accurate knowledge as to the life history of the insect vector. *Anopheles albimanus* is, so far as is known, the only efficient vector of malaria and, in breeding, is capable of adapting itself to an extremely wide range of local natural conditions. Larvae may be found below 2,500 feet throughout the island in almost every conceivable type of water deposit. Considering this characteristic along with year-round favorable temperature, and the location of homes near water, one may easily visualize the enormous task which mosquito control presents. In the Southern states of the United States and in many parts of the world anophelines favor certain places for daylight resting. Regular visits to such locations in the vicinity of control operations with recording of the number of anophelines found is a valuable check on the success of the control measures. To date no one has discovered the usual daylight retreat of the *Anopheles albimanus* in Haiti. Without this information one has to rely on evidence of larval infestation of suspected waters.

It would be beyond the scope of this article to outline a plan of action designed to solve the problems which the control of malaria presents. Results obtained in the past ten years indicate the wisdom of the methods employed. Although all of these results cannot be proved by statistics, yet there is sufficient information at hand to conclusively demonstrate a decline in malaria among certain groups of the population and in most of the larger towns and cities. These figures have been published in the Annual Reports of the Director General, National Public Health Service of Haiti, and need not be repeated at this time.

ON ANOPHELES PSEUDOPUNCTIPENNIS AND ITS RELATION TO MALARIA IN MEXICO*

By CARLOS C. HOFFMANN, M.D.,
Mexico City, Mexico

Of the ten species of Anopheles found in Mexico, four only are of practical importance as vectors of malaria in this country. Among the species which have a North American center of distribution only two have to be considered: *A. quadrimaculatus* and *A. crucians*, whereas of the South American fauna *A. albimanus* and *A. pseudopunctipennis* act as vectors. The influence of the two latter species on the development of epidemic outbreaks is preponderant in nearly all malarious regions of the country. The same can be said in regard to endemic recrudescences.

Anopheles crucians is found only in the regions of the brackish waters along the Gulf coast. Although it undoubtedly takes part in the transmission of malaria in the states of Tamaulipas and Veracruz about as far south as the port of Tuxpan, its importance in these states lies far behind that of *A. albimanus*, which finds ideal conditions for unlimited multiplication in these regions. Further south I have found *A. crucians* as an inhabitant of mangrove districts on the coast of Campeche and Yucatan. It is practically the only species of Anopheles in those parts, because the high salt concentration of the breeding places and the complete absence of rivers present conditions almost prohibitive for the existence of other species. Since *A. crucians* remains nearly exclusively restricted to the sparsely populated mangrove districts, it can play but little part in the periodically appearing epidemics in the harbors of Yucatan.

On the Gulf coast, the region permanently infested with *Anopheles quadrimaculatus* extends as far south as Tuxpan. Although I have found this species as far south as the valley of the Papaloapan River, its appearance there was always transient and no indication of a permanent settling could be observed. In the central parts of the country *A. quadrimaculatus* reaches considerably more southward, infesting abundantly the State of Guanajuato and contiguous regions of Jalisco and Michoacan, and extending as far south as to the Valley of Mexico. On the coast its principal time of multiplication is during the winter months, exhibiting there, as I have already emphasized during other occasions, a marked zoophilism. It is more important as a vector in the interior regions of the country, where it is found side by side with *A. pseudopunctipennis*. For reasons which will be discussed later, it has at present

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*From the Department of Public Health, Republic of Mexico.

to be considered the principal vector of malaria in the capital.

Anopheles albimanus exhibits all the characteristics of a species adapted to a hot and moist climate. In the Gulf coast it extends from Quintana Roo to the mouth of the Rio Bravo. In the regions situated between the southern parts of the state of Taumaulipas and the Champoton River in Campeche it is the most predominant anopheline species and the principal vector of malaria. In some localities it is even the only one. Within the extensive area it inhabits not only the littoral parts, but extends inwards along the basins of the rivers to an altitude of 400 meters, penetrating deeper into the valleys of the southern states than it does along the rivers of the north. The farther it goes off from the coast or settles in higher altitudes the more it loses its numerical supremacy and epidemiological importance. According to its tropical and hygrophile character, its principal time of development and vector activity is during the rainy season. It suffers an extraordinary reduction everywhere during the dry winter months, when it even may disappear completely from certain regions.

On the coast of the peninsula of Yucatan, where rivers and brooks are absent, the living conditions for *A. albimanus* are very distinct from those present in the other Gulf states, where rivers are plentiful. In Yucatan this species is found in isolated parts near the coast, where dense forests are absent and where during the rainy season swamps of sweet or slightly salty water are formed. Artificially favorable conditions are created here near the villages and ranches by the construction of water deposits used for irrigation, drainage or water supply. Especially these artificial breeding places constitute, in my opinion, the main danger for the human settlings in Yucatan and are responsible for the serious outbreaks of epidemic malaria among them. The climatic character of the greater part of Yucatan is decidedly unfavorable for malaria and its presence there is possible only through a species of Anopheles which easily adapts itself to artificially created conditions. The peninsula of Yucatan is the only part of Mexico where I found the larvae of *A. albimanus* within artificial water deposits, especially in the tanks used for irrigation of gardens and orchards (Campeche and Merida). *A. albimanus* has to be considered as the only species responsible for the epidemics in Yucatan. These epidemics, as I learned from personal experience, are always coincident with an enormous multiplication of this species.

Along the Pacific *A. albimanus* is found over a large part of the littoral region, from Guatemala to the southern districts of the State of Sinaloa, but its distribution here is not so regular and its number far less predominant than in the Gulf coast. It is found especially during the rainy season, exhibiting a decided tendency to distribution over circumscribed areas where conditions for its development are favorable. This difference of its distribution in the Gulf states and in those of the Pacific is explained by the dryer climate of the latter. It is for the same reason that its zone of activity is nearly exclusively limited to the littoral lowland. Only along the Santiago and Balsas Rivers it penetrates deeper into the country.

From the survey given on the preceding pages we see that the Nearctic species *A. crucians* and *A. quadrimaculatus* have a relatively small part in the transmission of malaria in Mexico, and that, on the other hand, the regions of dangerous activity of the southern *Anopheles albimanus* is restricted to well limited areas of the littoral, moist and hot lowlands and regions immediately adjacent. These regions constitute, however, only a small part of the endemic zones of malaria which are not limited to the hot and moist country, but extend over an enormous area of the central part of the country, which is characterized by a more or less dry climate, not sparing the high valleys 6,000 to 7,000 feet above sea level. In spite of Mexico's being a dry country *par excellence*, the control of malaria within its arid regions is of vital importance and causes constant preoccupation to the health authorities. The southern parts of the State of Puebla, the State of Guerrero, Sinaloa and others are malarious zones of prime importance which, in their rural districts, show a parasitic index of 50 per cent and even more, percentages which certainly are not lower than those observed in the hot and moist lowlands of the Gulf states.

The serious infestation with malaria of the interior parts of Mexico can only be understood by the presence of very large numbers of *A. pseudopunctipennis*. This species is perfectly adapted to dry climates and is decidedly xerophile in all its biological manifestations. Among the Mexican species of Anopheles it is the only one which, during the excessive dryness of the winter months, which prevails over large areas of the south and west of the country, does not stop its activity. On the contrary, the dry season coincides in many parts with the principal period of abundant multiplication of this species. For this reason *A. pseudopunctipennis* is the principal cause of winter malaria, so frequent in Mexico, and in the southern and western parts it is the only species which can be made responsible for it during that time of the year.

A. pseudopunctipennis is found in all parts of Mexico where the essential conditions for its procreation are given. It is in clear and pure, flowing or stagnant waters, especially where the waters contain a flora of green algae. Only altitudes over 6,000 to 7,000 feet are free from it as well as the very moist regions of the south and the southeast.

In the littoral zone of the Pacific, *A. pseudopunctipennis* extends along the entire coast from Guatemala to California. Its subspecies, *franciscanus* McCracken, inhabits only the northern part, extending as far south as into the northern districts of the State of Sinaloa. During the rainy season it enters in competition with *A. albimanus* in many parts of the littoral coast districts, but while the larvae of *albimanus* are found preferently within permanent stagnant fresh waters and

also within brackish ones, the breeding places of *A. pseudopunctipennis* are constituted by temporary rain water pools, flooded meadows and river banks. By the local prevalence of the one or the other of these conditions, the numerical prevalence of *A. albimanus* or *A. pseudopunctipennis* is decided during the rainy season.

In those parts of the west coast of Oaxaca, Guerrero, Colima, Nayarit and many parts of Sinaloa, where a decided preponderance of *A. albimanus* is observed during the rainy season, the number of this species begins to diminish gradually beginning with October, whereas *A. pseudopunctipennis* appears in ever-increasing numbers, predominating during the whole dry season until the months of April or May.

The high endemic parasitic index which is found practically along the whole littoral zone of the Pacific, especially in Nayarit and in the sugar plantations of Sinaloa, can therefore be attributed to the activity of both forementioned species. The epidemic peaks of estivo-autumnal fever, however, appearing in these regions in December and during the first months of the year, are principally due to *A. pseudopunctipennis*. Tropical fever is the most frequent form of malaria along the coast of the Pacific; the endemic index of tertian parasites is as a rule higher than that found on the Gulf coast. The parasite of quartan fever I have found in only a small percentage.

Already at a few miles inside of the coast *A. albimanus* is found in steadily diminishing numbers also during the rainy season and *A. pseudopunctipennis* begins to dominate more and more as one goes farther inside. In all the west coast states this species is the only transmitter which has to be considered from a practical point of view, within the entire zone which extends between the littoral zone proper and the slopes and valleys of the western mountainous regions. Numerous small rivers which rise in the mountains and flow to the Pacific offer adequate breeding conditions. On different localities I have observed large quantities of larvae of *A. pseudopunctipennis* between stones and small sand bars along the banks of these rivers, without the presence of a noticeable vegetation of algae or other aquatic flora.

On some southern slopes of the Sierra where, during the summer months, abundant rainfall causes the rivers to rise, converting them into rapidly flowing streams, adequate breeding places can exist along these rivers during the dry season only, all anopheline activities disappearing with the onset of the heavy tropical rains. These conditions can be observed in the coffee zone of the Sierra of Soconusco in the State of Chiapas, where the annual precipitation amounts to 4.75 meters of rain and where a well defined dry season is present. It is very significant that *A. pseudopunctipennis*, a xerophile species, has invaded these highly humid regions, but its activity is entirely limited to the dry months, and active malaria is observed only during this part of the year.

Not infrequently I could observe small foci of endemic malaria in isolated villages of the western mountainous regions. The people of these villages descend during a certain time of the year to the coast as temporary laborers on the haciendas. On account of this, malaria was in recent times carried from the sugar plantations situated in the littoral lowlands of Sinaloa into the interior of the State, as far as to the limits of the States of Chihuahua and Durango.

The whole part of Mexico which is called interior and which is situated between the western range of mountains along the Pacific and the eastern range along the Gulf can properly be divided into three malarious areas, all three inhabited by *A. pseudopunctipennis* but exhibiting different biological and epidemiological conditions.

(1) The southern zone, separated from the north by the high transverse volcanic range of mountains, comprises the State of Morelos, the southern parts of the States of Puebla, Mexico, and Michoacan and the States of Guerrero, Oaxaca and Chiapas.

(2) The central zone, comprising essentially the States of Hidalgo, Queretaro, Guanajuato and Jalisco, the northern parts of Michoacan and Mexico and the Federal district.

(3) The northern zone, comprising the dry territory north of the second zone up to the Rio Bravo.

The southern zone, having an essentially dry climate, offers ideal conditions for the life of *A. pseudopunctipennis*. It is the predominant anopheline species and practically the only transmitter of malaria. The high transverse mountain range which separates this zone from the north constitutes the southern limit of distribution for many insects of northern origin and forms also a barrier to the northern anopheline species. Besides *A. pseudopunctipennis* the southern zone harbors also *A. vestitipennis, A. punctimacula* and *A. apicimacula*, but the latter three species can practically be neglected as vectors of malaria. Their distribution is almost limited to the sylvan regions of the Isthmus of Tehuantepec and Chiapas and to the limitrophe districts of Veracruz.

The most malarious regions extend along the rivers, the tributaries of which rise in the high mountains and have clear water also during the dry winter months. In these rivers a notable concentration of breeding places of *A. pseudopunctipennis* is observed, especially within shallow water pools which are more or less cut off from the current, owing to the sinking of the river level during the dry season. These pools contain nearly always an abundant flora of green algae. But even within the free floating parts of the river, breeding places of *A. pseudopunctipennis* are observed in large masses of green algae, which from between the stones extend to the surface of the water. During the rainy season the majority of these rivers, and especially their small tributaries, offer much less favorable conditions for larvae. On account of the very heavy rains they rise considerably and are transformed into rapidly flowing waters which remove the larvae. Besides, their

water becomes very muddy and unsuitable for the breeding of *A. pseudopunctipennis*. For this reason the breeding places disappear during the rainy season more or less completely from the river basins and change to temporary water pools, irrigation systems and rice fields.

The majority of the villages in the States of Puebla, Morelos and Guerrero are situated along rivers. It is easily understood, therefore, that malaria takes a greater toll among them during the dry winter months with their notable concentration of breeding places along the river banks than during summer, when they are scarcer, widely separated and farther off from the villages.

Tertian fever undoubtedly is the predominant form in the whole southern zone, but the proportion between tertian and estivo autumnal is quite high in many places, especially along the whole system of the Balsas River. According to my observations during the last six years, the proportion between tertian and estivo-autumnal infections in the valleys of the southern zone is 3:2. In the higher regions of Oaxaca and in the dry anterior of Chiapas the estivo-autumnal form is considerably less frequent. I am not able to give definite information in respect to quartan fever. I found it as a rule in localized, circumscribed districts, where occasionally the proportion between tertian and quartan attained an index of 3:1.

In the central zone the situation in respect to malaria is quite different. Here with the exception of *A. pseudopunctipennis*, the southern anopheline species are absent, their place being taken by the northern species *quadrimaculatus* and *punctipennis*. In the central part of the zone, with the State of Guanajuato as its center, between altitudes of 1,600 to 2,200 meters, the two species participate as vectors of malaria, the one or the other species predominating according to the biological conditions offered by the waters. Eastward and westward from this center *quadrimaculatus* begins to disappear, leaving the field entirely to *pseudopunctipennis* in the malarious regions of Jalisco and the basin of the Lerma River in the west, and in the very hot and dry territory of the State of Hidalgo in the east.

In the valley of Mexico at an altitude of 2,200 meters the two species are found. In the suburbs of the capital and in the surrounding villages *A. quadrimaculatus* is found nearly exclusively. *A. pseudopunctipennis* has retired more and more from the urbanized regions to rural districts, which offer more numerous and more adequate breeding places with clear water. The procreation of *A. quadrimaculatus* continues uninterrupted during the whole winter in the high Valley of Mexico. In the case of *A. pseudopunctipennis* one notices a cessation of its activity for 4 to six weeks in cold winters in the beginning of the year.

In the central zone tertian fever is the most predominant one and in the higher altitudes it is practically the only form of malaria found. Cases of estivo-autumnal are seen very rarely in the Valley of Mexico. More frequently they are found in certain parts of Michoacan, in the basin of the Lerma River and in the hot country of Hidalgo, but the local indices never attain the high proportions found in the southern zone.

The northern zone has its own peculiar characteristics. It is excessively dry, semi-arid or completely barren and is nearly completely devoid of permanent streams and rivers. The majority of these rivers rise in the Sierra, but they have water only in their upper part. Reaching the hot and dry plains, they sink under the ground and follow a subterranean course, forming the so-called "rios secos" (dry rivers) so characteristic of this zone. At a first glance it would seem rather improbable that the beds of these rivers, which carry waters only after heavy rain and during a short period of the year, would constitute one of the most serious problems in respect to malaria in the northern zone. The danger arises from filtrations which take place into the beds of many of these dry rivers. Very clear waters rise in the beds, running for about a hundred yards, only to sink under the ground again, or more or less permanent pools are formed. These waters form ideal breeding places for *A. pseudopunctipennis* and *A. punctipennis*. For *A. quadrimaculatus* the region seems to be too dry and the species is found only in the borders of the zone.

A second interesting condition of the zone is the adaptation of *A. pseudopunctipennis* to artificial water deposits. I quote in this respect especially the city of Monterrey. This City suffers frequent epidemic outbreaks of malaria coincident with an abundant development of *A. pseudopunctipennis*. The search for the cause of this development revealed to me always a very heavy infestation with larvae of *A. pseudopunctipennis* of the filtration water in the dry bed of the Santa Catarina River, as well as of the fountains and the tanks in the gardens and patios of the houses. It is evident that the control of malaria under such conditions is relatively easily accomplished by proper methods applied along the river beds and by rigid health board rules in respect to all artificial water deposits, which brought prompt relief during our campaign in 1928.

Within the dry northern zone malaria has a far wider distribution than has generally been supposed. *A. pseudopunctipennis* is practically the only vector of malaria and a rough estimation of the infection may be obtained from the predominance of the latter species or of *A. punctipennis*. Villages of the north which show only *A. punctipennis* are practically free of malaria. They are generally situated at higher altitudes (Saltillo, etc.). Even in the central parts of the most dry and most arid regions, as for instance in the State of San Luis Potosi and the near-by districts of Tamaulipas, I found larvae of *A. pseudopunctipennis* with certain regularity within isolated natural springs ("ojos de agua") and draw wells of the ranches.

Tertian malaria predominates absolutely in this

northern zone. During our survey in the interior of the States of Nuevo Leon and Tamaulipas, tropical malaria did not even attain 10 per cent of the cases of tertian.

As already mentioned, *A. albimanus* predominates in the littoral zone of the Gulf not only numerically, but also as a transmitter of malaria. Besides from this species *A. vestitipennis, A. pseudopunctipennis, A. quadrimaculatus, A. crucians, A. punctipennis, A. punctimacula, A. apicimacula, A. cruzii* and *A. argyritarsis* are represented. Of the latter species, *A. pseudopunctipennis, A. crucians* and *A. quadrimaculatus* play the role of transmitters, but only a secondary one. The malaria curve rises and falls according to development and abundance of *A. albimanus*.

A. pseudopunctipennis is found in the entire littoral zone north of Veracruz and a short distance south of that City. During summer it disappears nearly completely, but reappears in considerable numbers in winter, attaining in the northern part of the coast predominance over all the other species. Further south it never attains such high proportions. In the dryer prairies and bush regions between the littoral zone and the slopes of the eastern Sierra it is found more abundantly, becoming more important as a vector of malaria. I have never observed *A. pseudopunctipennis* in the region of the large rivers in the northern part of the State of Veracruz, in Tabasco and Campeche, and I doubt that it exists there. In the entire zone estivo-autumnal malaria predominates. In the littoral region proper very low indices of tertian cases are found, but farther inside their number increases steadily, reaching more or less the proportions which we have observed in the southern interior zone.

It is interesting that *A. pseudopunctipennis* has also invaded the villages of Yucatan, which are situated inside of the littoral zone. In Merida we found frequently during the dry first months of the year the same water deposits populated by larvae of *A. pseudopunctipennis* which, during the rainy season, harbor *A. albimanus*, but I do not think that *A. pseudopunctipennis* has at present any decided influence on malaria there.

For an easier orientation I add a chart. I show the seven malarious zones which I distinguish in Mexico. The chart illustrates the species of Anopheles found in each zone, the species which act as transmitters and the form of malaria which predominates. The chart illustrates very well the enormous importance of *A. pseudopunctipennis* as a vector of malaria in the country.

Malaria Zone	Anopheles Found in the Zone	Active Transmitters in the Zone	Predominant Forms of Malaria
		A.—Littoral of the Pacific	
I. Littoral zone of the Pacific	A. pseudopunctipennis A. albimanus	A. pseudopunctipennis A. albimanus	Estivo-autumnal fever predominant; higher proportions of tertian fever than on the Gulf coast
II. Interior zone of the Pacific	A. pseudopunctipennis	A. pseudopunctipennis	Estivo-autumnal and tertian fevers in different proportions; as a rule, the tertian fever predominates
		B.—Interior	
III. Southern zone	A. pseudopunctipennis A. vestitipennis A. punctimacula A. apicimacula	A. pseudopunctipennis	Tertian form predominates. Percentage between tertian fevers and estivo-autumnal up to 3:2
IV. Central zone	A. pseudopunctipennis A. quadrimaculatus A. punctipennis	A. pseudopunctipennis A. quadrimaculatus	Tertian form predominates. Very slow proportions of estivo-autumnal
V. Northern zone	A. pseudopunctipennis A. punctipennis (A. quadrimaculatus)	A. pseudopunctipennis (A. quadrimaculatus)	Tertian form predominates, estivo-autumnal fever to 10 per cent of tertian cases
		C.—Littoral of the Gulf	
VI. Littoral zone of the Gulf	A. albimanus A. pseudopunctipennis A. quadrimaculatus A. crucians A. punctipennis A. vestitipennis A. punctimacula A. apicimacula A. cruzii A. argyritarsis	A. albimanus A. pseudopunctipennis A. quadrimaculatus A. crucians	Estivo-autumnal fever predominant. Tertian form in different proportions, higher in the interior districts
VII. Zone of Yucatan	A. albimanus A. crucians A. pseudopunctipennis A. vestitipennis A. apicimacula A. punctimacula	A. albimanus A. crucians A. pseudopunctipennis	Estivo-autumnal fever predominates. Tertian form in different proportions

DISCUSSION (*Abstract*)

Dr. Francisco de P. Miranda, Mexico City, Mexico.—The Republic of Mexico has thirteen different climates. The northwest region has the same climate as California, a Mediterranean temperate climate. Two chains of mountains divide the Republic in two coastal regions and that of the high plateau in the middle. In this elevated portion lies Mexico City and other cities like Puebla, more than 7,000 feet above sea level. On account of the great altitude there is very little malaria in that part of the country. The States of Veracruz and Tabasco are tropical and have the highest malaria incidence. In the part where these two mountains unite there is a succession of volcanoes which extend from the Gulf of Mexico to the Pacific Ocean. Geographically, these volcanoes separate North America from Central America. The State of Chiapas and part of that of Oaxaca have the same climatic conditions as has Guatemala and other Central American countries. The State of Yucatan has the same climate and structure as Cuba.

In most of these discussions, malaria in the high plateau is the problem which you do not have in the United States. Beginning with Monterrey and going up to Saltillo, the problem is different from the true tropical regions where the *albimanus* has great importance. *Pseudopunctipennis* that can live in higher altitudes becomes the most important vector.

Dr. H. C. Clark, Panama, R. de P.—My experience has been largely confined to the coastal plains of Colombia, Panama, Costa Rica, Honduras, Guatemala, Cuba, Jamaica and Haiti. The highlands of Costa Rica and Haiti have revealed the breeding of *A. albimanus* at an elevation of 3,000 feet in Costa Rica and at 1,500 feet in Haiti. Other mosquitoes are more abundant at these levels, but the presence of *A. albimanus*, even in small numbers, should be kept in mind as an important vector. Where clean running water is exposed to sunlight and the barrels or troughs collect algae on the bottom and sides, *A. albimanus* can breed. We have found them under such artificial conditions.

It is frequently very difficult to correlate the malaria parasite index in a given region with the mosquito flights and data collected from breeding grounds near by. We prefer to rely on the dissection of mosquitoes trapped in human habitations.

I am surprised to hear that *A. pseudopunctipennis* is considered a vector in the high tablelands of Mexico. We have this mosquito in the countries I have visited, but it seems to breed abundantly only in dry season. It bears the reputation of not entering human habitations, but we have made large catches in camp quarters of well constructed thatch roof and cane walls in dry season. As many as 77 on one visit were caught in a room where three people slept. They do not feed on the human being in the vigorous manner noted in experiments with *A. albimanus*. *A. pseudopunctipennis* is a very lazy, clumsy feeder and we have never been able to infect it in experiments on human or monkey malaria. Others, we know, have reported successful feeding results with this mosquito, but we do not consider it an important vector in our part of the world.

Mr. W. H. W. Komp, Sanitary Engineer, U.S.P.H.S., Ancon, Canal Zone.—The report of *A. quadrimaculatus* in the environs of Mexico City is particularly interesting, as it does not fit in with our knowledge of the distribution of this species. *Quadrimaculatus* is found as far south as the valley of the Rio Grande, at Brownsville, but has not been taken further south, to my knowledge. On the other hand, we should expect *Anopheles maculipennis*, a cold-water breeder, to be found in the mountainous regions of Mexico, as I have taken it in Utah and New Mexico at considerable elevation, where it was not associated with *A. quadrimaculatus*. In view of the close similarity of these two species, it is possible that Dr. Hoffmann may have made an error of identification.

Dr. D. M. Molloy, Guatemala City.—Conditions in the highlands of several of the Central American countries are very similar to those described for certain sections of Mexico in Dr. Hoffmann's paper. Entomological surveys made in Guatemala during the past year have indicated that *A. pseudopunctipennis* is practically the only Anopheles present in the highlands of the interior of Guatemala. Malaria is present at an altitude of about 5,000 feet, recently appearing in quite sharp outbreaks in the outskirts of Guatemala City. In the environs of Guatemala City Anopheles have never been taken in sufficient numbers to account for this malaria except *A. pseudopunctipennis*. *A. albimanus* was recently taken at an altitude of 4,500 feet near Guatemala City. What would seem to be a new species of Anopheles, closely resembling *A. pseudopunctipennis*, was recently described by Giaquinto in the Bulletin of the National Health Department of Guatemala. It would appear that this Anopheles is a vector of malaria since it was the only Anopheles taken in a small village about eight miles distant from Guatemala City, where a sharp outbreak of malaria occurred. In practically all of the highlands of Guatemala *pseudopunctipennis* abounded during last year, special climatic conditions existing throughout the entire year, the year having been probably the driest which has been known for twenty years. As has been found to be the case elsewhere, years of exceptionally light rainfall favor the production of Anopheles in the highlands, while the reverse is the case when a normal rainfall occurs. Very sharp outbreaks of malaria occurred in the towns and villages on the shores of Lake Atitlan, 5,200 feet above sea level, during last year. Extensive anopheles surveys on the shores of the lake failed to reveal the presence of any Anopheles except *pseudopunctipennis*. These surveys have been continued during the present year and no other Anopheles has been taken. It would therefore appear that *pseudopunctipennis* is the most important vector of malaria in the highlands of Guatemala. It has been shown to be the only vector of any importance in certain parts of the Argentine, and I can see no reason why this should not hold for the highlands of Central America and Mexico.

A. albimanus is constantly encroaching on the highlands of Central America. It has recently been taken in the immediate vicinity of Guatemala City, but not in sufficient numbers to account for the malaria present there. In Costa Rica *albimanus* was taken in large numbers in several towns near San Jose, and was undoubtedly responsible in large measure for the outbreaks of malaria which occurred in these towns, although *pseudopuntipennis* was also present in considerable numbers. Everyone knows, of course, that *A. albimanus* is the most important vector in the coastal plains of the American tropics. Our experience in the highlands of Central America has convinced me that *pseudopunctipennis* is the most important vector in the highlands of these countries. This would seem to be

the case in Mexico where, according to Dr. Hoffmann, *pseudopunctipennis* was the only Anopheles taken in regions between five and seven thousand feet in altitude where malaria is present.

Dr. M. A. Barber, New York, N. Y.—I have recently had some experience in the Rio Grande Valley of New Mexico, where *pseudopunctipennis* and *maculipennis* are the chief species of Anopheles. My conclusion, as well as that of Mr. Komp, who worked with me there, was that *maculipennis* is the chief vector of malaria in that valley.

ANTIMALARIAL VALUE OF CINCHONA ALKALOIDS OTHER THAN QUININE*

By W. T. Dawson, M.A.,†
Galveston, Tex.

The question may be asked, "Why should we concern ourselves with the use in malaria of any cinchona alkaloid other than quinine, since quinine is certainly 99.9 per cent efficient as a remedy when intelligently and perseveringly used?" I shall try to answer that question.

Quinine is one of four principal crystallizable alkaloids contained in cinchona barks. Of these, the first to be discovered was cinchonine in 1810, quinine being isolated ten years later. Quinine sulphate is mentioned in the "U. S. Pharmacopoeia," edition II, 1830. In the third edition, 1851, cinchonine sulphate became official, and in the sixth (1882) cinchonidine sulphate and quinidine sulphate were added, having been definitely distinguished by Pasteur in 1853. There was a very practical reason for these inclusions. All sorts of cinchona barks were on the market and all four alkaloids were produced in considerable quantity. As all four were reported in medical literature to possess the property of terminating the paroxysms of malaria, all four became official. It is interesting to go back into the older clinical literature and read some of the evidence upon which our predecessors based their opinion that not one but several cinchona alkaloids were to be considered effective antiperiodics. Thus we can find articles on cinchonine sulphate by William Pepper,[1] in 1853, and A. P. Turner,[2] in 1864, in the *American Journal of the Medical Sciences*, the former considering cinchonine equal to quinine, the latter agreeing, provided cinchonine were used in "slightly larger doses." One of the largest scale experiments in comparative therapeutics ever undertaken was that of the Madras Chinchona Commission[3] of 1866-68, in India, which tried to compare the antimalarial activity of quinine, quinidine, cinchonidine and cinchonine of good purity,[4] in which 3,617 patients were treated, at least 750 with each alkaloid. The lowest percentage of cures, indicated by cessation of paroxysms, was 97.6, with cinchonine, and the Commission therefore showed that any of the four common cinchona alkaloids was an excellent antiperiodic. The data do not really enable a comparison of the four alkaloids, since almost 90 per cent of the cases treated were quotidian fevers and, in the then ignorance of the existence of malarial parasites, possibly a few cases of fevers not truly malarial may have been included.

An economic revolution in the cinchona trade[5] occurred between 1880 and 1911, and cinchona barks with high content of alkaloids other than quinine have practically disappeared from the markets of the world. In 1880 probably 85 per cent of the bark still came from South America,[5] and bark in general was relatively much lower in quinine and higher in other alkaloids than now. Java was a very minor competitor, but under the guidance of Moens[6] was studying quinine production scientifically. In 1879, Moens was planting seed from trees which had shown not less than 9 per cent of quinine in the bark,[6] against an average of less than 2 per cent in the current bark supplies.[5] After 20 years of bitter competition, over-production and low prices, the less scientifically managed plantations elsewhere had disappeared as competitors, and in 1911 Java supplied about 95 per cent of the world's bark,[5] the average quinine content of which had risen to over 3 per cent and is now, with Java still far in the lead, nearly 5 per cent. As the quinine percentage rose, the percentage of other alkaloids fell, and the production of the latter has decreased to the point where for every seven tons of quinine only about one ton is now produced of the other three alkaloids combined. It has become rather unfashionable than incorrect to use these minor alkaloids in the treatment of malaria.

Since we have come to know the cause of malaria, we have had in the parasite a test object in chemotherapeutic investigation of the subject. The comparison of the parasiticidal effects of different cinchona alkaloids has engaged the attention of a number of investigators, with varying claims resulting. Thus Mac Gilchrist[8] ranked cinchonine above quinine, while Giemsa and Werner,[9] using smaller doses, considered cinchonine much inferior. Most observers appear to have thought quinidine equal or superior to quinine and the Malaria Commission of the League of Nations has accepted their practical equivalence.[10] Cinchonidine has not been so much investigated, perhaps because it is difficult to purify from quinine, of which about 10 per cent is ordinarily found as an impurity. So far as benign tertian malaria is concerned, the work in India of Sinton,[11] who is an honorary member of this Committee, led him to conclude that the percentage of relapses is likely to be about the same, whichever of the four common alkaloids is used in the course of treatment. With cinchonine sulphate costing just now about 40 per cent less than quinine sulphate, some use of cinchonine might be advisable in definitely diagnosed *P. vivax* infections. But the supply available, about 30 tons[12] annually, is small as compared with the 600 tons of quinine,[5] and any extensive demand would

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†Professor of Pharmacology, University of Texas School of Medicine.

cause a prompt rise in price of cinchonine. As regards comparisons of the alkaloids in estivo-autumnal infections,[13] quinidine appears to be equal to quinine, but cinchonine and cinchonidine are perhaps somewhat inferior in small doses. The statistics are not so extensive as with benign tertian infections, possibly because the investigators in India, who have been the most diligent workers in the field, appear to have found quinine very highly effective in preventing relapse with rather short courses of treatment, much more so than in benign tertian infections.[14] Quartan fevers yield to any of the four alkaloids,[15] possibly like benign tertian infections. It is evident that for any fair comparison large numbers of patients should be treated with each alkaloid under controlled conditions.

There is at least one practical application of the foregoing review. In order to grasp it one must recall a little chemistry. The four common cinchona alkaloids are really two pairs of optical isomers, quinine and quinidine forming one pair, cinchonidine and cinchonine the other.[16] Quinine and cinchonidine are levorotatory, quinidine and cinchonine are, respectively, their dextrorotatory isomers. In a small proportion of cases of malaria the treatment is complicated by the occurrence of an unusual and intolerable reaction to quinine, taking the form of coryza, urticaria or even acute dyspneic attacks. Evidence[17] is accumulating that a dextrorotatory cinchona alkaloid such as quinidine or cinchonine may in such cases be substituted for quinine and such unpleasant side-effects be thereby avoided. Of these two possible substitutes, quinidine appears to have better endorsements as to its antimalarial activity than cinchonine.

Another suggestion that might prove of some practical value is that quinidine might be given a trial in the rare cases of malarial infection which appear to be rather resistant to quinine or to relapse readily.

Research upon the chemistry of the four common cinchona alkaloids has shown that each contains as an impurity a hydroalkaloid of very similar chemical, physical and physiological properties. Thus we may have present in quinine about 2 per cent of hydroquinine,[18] in quinidine up to perhaps 30 per cent of hydroquinidine,[18] in cinchonine up to 15 per cent of hydrocinchonine,[19] and in cinchonidine 8 per cent of hydrocinchonidine.[18] The chemical relation is very simple. If the common alkaloid be given the abbreviated formula B. CH: CH_2 that of the corresponding hydroalkaloid[16] becomes B. $CH_2.CH_3$. Hydroquinine[20] and hydroquinidine[9] have both been shown to possess high antimalarial activity. Some doubt has, however, been cast upon the value of hydrocinchonine[9] in malaria. Hydrocinchonidine had apparently not previously been tested. A Texas-Louisiana group of medical teachers and practitioners has been interested in testing out the effect of this hydrogenation[16] of the common cinchona alkaloids upon the antimalarial activity. We are not yet quite ready to make complete reports. But we have records of cases of malaria treated with hydroalkaloids which show that a few days' treatment with any one of them is capable of producing disappearance of fever and of parasites. This work has some practical importance, since Dr. Paul Rabe, the eminent German chemist, has reported (Ber. 64:2487) that he has succeeded in the complete synthesis of hydroquinine and hydroquinidine.

Including hydrocinchonidine and hydrocinchonine, some sixteen closely related natural or synthetic cinchona alkaloids have now been shown to possess definite antimalarial activity, but the results obtained have not been sufficiently promising in the case of any of these to justify urging a general substitution for the time-tested quinine of a more expensive substance. A list of all the cinchona alkaloids tested in malaria follows.

Cinchona planting has now almost died out in the Americas, despite the fact that Ecuador, Peru and Bolivia were the original sources. Colombia dominated the cinchona trade in 1880 and shipped to Europe 3,000 tons of bark.[5] Jamaica in the same year shipped a few tons.[5] Possibly some Central American or Mexican areas might prove suitable also. The elevation should be 1,000 to 5,000 feet, the rainfall about 75 to 180 inches per annum.[27] In Java good results are obtained[6] on soils "of porous structure with much humus and of recent volcanic origin." Sample plots of one to ten acres will yield the neces-

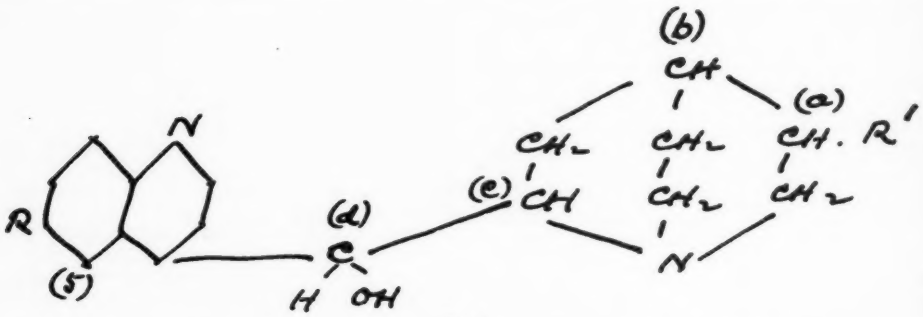

Fig. 1

General formula, cinchona alkaloids. The abcd carbon atoms asymmetric, probably dddd in d-isomers below, ddll in l-isomers.[21]

Table I

CINCHONA ALKALOIDS EFFECTIVE IN MALARIA

L-Isomer	D-Isomer	R	R^1
Cinchonidine	Cinchonine	H	$CH{:}CH_2$
Hydrocinchonidine	Hydrocinchonine	H	CH_2CH_3
Cupreine[22]		HO	$CH{:}CH_2$
Quinine (methylcupriene)	Quinidine	CH_3O	$CH{:}CH_2$
Ethylcupreine[22]		C_2H_5O	$CH{:}CH_2$
Propylcupreine[22]		C_3H_7O	$CH{:}CH_2$
Hydroquinine (Methylhydrocupreine)	Hydroquinidine	CH_3O	CH_2CH_3
Ethylhydrocupreine[23]		C_2H_5O	CH_2CH_3
Isopropylhydrocupreine[23]		C_3H_7O	CH_2CH_3
Isoamylhydrocupreine[23]		$C_5H_{11}O$	CH_2CH_3
Aminohydroquinine[24] (NH_2 group at 5)		CH_3O	CH_2CH_3
Ethylquitenine[24]		CH_3O	$COOC_2H_5$
B. Ineffective so far as tested.			
Quitenine[25]		CH_3O	COOH
Quinicine[26] (Molecule as of quinine internally rearranged[16])		CH_3O	$CH{:}CH_2$

sary data as to desirability in four years of careful cultivation.[27]

It would presumably be perfectly possible to produce bark with high quinidine, cinchonidine or cinchonine yields if desired. Thus a variety of C. ledgeriana, called "chinidinifera," has shown in recent Dutch analyses nearly 4 per cent quinidine,[7] against 0.2 per cent or less in current bark supplies, mainly from Java.[5] Detail of analysis[7] of chinidinifera ledgeriana bark showed percentage (compared with 1929 average commercial bark in brackets[5]): quinine 1.86 (4.935), quinidine 3.86 (0.140), cinchonidine 0.15 (0.384), cinchonine and amorphous 1.81 (0.288 and 1.179).

SUMMARY

Extensive investigations have shown that quinine and quinidine are of practically equal value in malaria, and that all four common cinchona alkaloids are of approximately equal value in chronic benign tertian malaria.

In cases of quinine idiosyncrasy, taking the form of urticaria, coryza or dyspneic attacks, quinidine or cinchonine may be given a trial with fair prospects of avoiding the unpleasant side effects, and especially in the case of quinidine, security as to therapeutic efficacy of the treatment.

Preliminary observations indicate that hydrocinchonidine and hydrocinchonine as well as hydroquinine and hydroquinidine possess definite antimalarial activity, a result of some theoretical importance.

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DISCUSSION (*Abstract*)

Dr. Charles T. Stone, Galveston, Tex.—It has been an interesting and profitable experience to conduct the treatment of patients with malaria in collaboration with Professor Dawson, using various cinchona alkaloids.

My first impression of the probable results of such treatment was that all of the alkaloids except quinine would prove to be relatively inefficient. If they had been effective they would have been at least mentioned in passing in text-books on medicine. In the early experiments, in order that no bias in favor of one alkaloid over another might possibly enter into the interpretation of clinical results of treatment, Professor Dawson by my request furnished me with capsules containing an alkaloid marked "A" or "B." Subsequently, this precaution was omitted. The drugs were administered to smear positive patients who were having typical paroxysms of chills and fever, and who were under careful observation in the hospital. Thus, it was possible to note not only the time of cessation of chills and fever, but also to observe the day on which the blood smear became plasmodium-negative.

The results were quite striking. In all of the alkaloids and hydroalkaloids used so far the paroxysms of chills and fever have been promptly controlled, and the smears have become negative for parasites. The average time necessary for the control of active symptoms and ridding the peripheral blood of plasmodia was two to four days. In all of these experiments an amount of the alkaloid equal to approximately ten grains of quinine sulphate was given daily. When the observations were completed, usually at the end of four days, the patients were placed upon ten grains of quinine sulphate daily for eight weeks. This was necessary to conserve the pure alkaloids obtained for experimental purposes for additional cases. The alkaloids studied up to the present time have been cinchonine and quinidine, while hydrocinchonine and hydrocinchonidine were also tried. In every respect, the action of all the substances is identical, and is comparable to that of quinine.

Perhaps the most important development in connection with the whole study from the clinical standpoint is the fact that those who have atopic reactions to levorotatory quinine may apparently be given the dextrorotatory alkaloids, quinidine and cinchonine, with safety. We have recently successfully treated a man sensitive to quinine, who developed tertian malaria, with cinchonine without any difficulty. It had previously been shown that he could also take quinidine without unpleasant effects, while quinine produced marked allergic reaction.

Most of the articles dealing with the therapy of malaria, in referring to the treatment of patients who have a so-called idiosyncrasy for quinine, recommend a host of remedies such as methylene blue, arsphenamine, oil of eucalyptus, atoxyl, or sodium cacodylate. All of these substances are, at best, poor seconds to quinine in their effectiveness in controlling malaria, while quinidine and cinchonine, with practically the same therapeutic efficiency as quinine, appear to be entirely harmless.

Dr. J. P. Sanders, Caspiana, La.—In a small series of cases in which I used hydrocinchonine and hydrocinchonidine in the treatment of malaria I found them to be of definite and positive value. However, I doubt that either is quite so potent as quinine or quinidine.

As to the value of quinidine in cases of idiosyncrasy to quinine, I believe there is little doubt. In the September 19, 1931, issue of the *Journal of the American Medical Association* I reported such a case with a complete history. The patient tolerated quinidine without difficulty and responded readily to treatment. In that paper I reported 38 other cases of malaria treated successfully with quinidine.

This year I have been treating a series of cases with quinine and quinidine trying to prove the value of quinidine relative to quinine. In a series of over 100 cases so far treated, one with quinine and the next with quinidine, I believe, though I have not compiled my results, that quinidine is equal to quinine in its antimalarial value.

I wish to ask Dr. Dawson in what way or by what mechanisms does quinine cure malaria?

Dr. William Krauss, Bolivar, Tenn.—My interest in the pharmacology of cinchona alkaloids dates back fifty years. In 1881 to 1883, I was a student assistant to Caspari at the University of Maryland. When quinine was selling at $5.00 and $6.00 an ounce, cinchonidine was largely used as a substitute because it was one-tenth as expensive. About that time, on account of the enormous prevalence of malaria in the South, Congress put quinine on the free list. Prior to that time exhaustive clinical tests seemed to reveal that the order of potency was: quinine, quinidine, cinchonidine and cinchonine. The latter was the basis of the first tasteless chill tonics. Quinidine is the most toxic.

I never will forget the derision with which Laveran's discovery was received at the University of Maryland by the gentlemen of the medical faculty.

Prof. Dawson (closing).—The mechanism of cure of malaria by quinine is, I think, unknown. We must consider various factors. The patient has, as a rule, some natural resistance to the infection, and cure, or at least remission, may occur in the absence of treatment (Boyd, "Introduction to Malariology," 1930, p. 23). Kirschbaum (Klin. Wchnschr., 2:1404, 1923) found tertian parasites incubated 5 to 24 hours with 1:10,000 quinine still infective to paretics, and a daily dosage of 90 grains (about 6 grams) of quinine sulphate produced a blood quinine concentration of only 1:60,000 (Ramsden, Lipkin and Whitley, Ann. Trop. Med. & Parasitol., 12:242, 1918-1919) so that the action of the ordinary 10-grain dose is probably indirect. Daily dosage of 90 grains is dangerous and does not prevent relapse (Ann. Trop. Med. & Parasitol., 12:71 and 11:417), while Osler found doses as small as 1 grain effective in stopping paroxysms in some cases. That other cinchona alkaloids cure malaria is of great scientific interest and must be considered in framing any adequate theory of the mode of action of quinine.

I am not urging that other alkaloids be used, but that quinidine is a possible substitute in some cases of quinine idiosyncrasy or intolerance.

I cannot explain the accusations of undue toxicity against cinchonidine and cinchonine.

Dr. William Krauss.—May I not be allowed the suggestion that at one time doctors often gave 60 grains at a single dose? And these doctors and their pupils are not all dead yet.

Prof. Dawson.—That may account for some of the complaints. Possibly the presence of toxic impurities may account for some others. Idiosyncrasy cannot be neglected as a factor. Extensive and careful observations in India and Italy have shown that cinchonidine and cinchonine possess high antimalarial activity and are not likely to be unduly toxic in 10-grain doses two or three times daily. With the present limited production of these other alkaloids as compared with that of quinine, they would undoubtedly become very expensive if there were any general demand for them.

OBSERVATIONS ON SOME FACTORS ASSOCIATED WITH THE BREEDING OF ANOPHELES MOSQUITOES IN NORTHEASTERN LOUISIANA*

By G. H. BRADLEY,†
Orlando, Fla.

INTRODUCTION

The fact that in a given locality Anopheles are found breeding in certain water areas and not in others, or sparsely in some areas and abundantly in others, has given rise to a considerable amount of investigation by numerous workers on the causes of this condition. The present paper is based on studies made of this problem in the northeastern part of Louisiana in what is known as the Louisiana Delta region. The contour of the land in this region is rather flat, accounting for poor natural drainage, and the formation of numerous shallow lakes in the lower areas, all of which are to a greater or lesser extent covered by tree growths. The streams are known as bayous and are very sluggish, having little or no current except after heavy rains, and are usually overgrown with trees and brush except in such areas as have been cleared of this growth. Branches of bayous which have become cut off from the main channel form sloughs, which are similar to the bayous except that they remain stagnant throughout the year and usually contain larger quantities of aquatic and semi-aquatic vegetation. All these areas have been found to be Anopheles producers.

METHODS OF OBSERVATION

Observations on the occurrence and abundance of Anopheles larvae at selected points in these water areas were made monthly from May to September, inclusive, during the years 1928 and 1929. The rate of occurrence was determined on the basis of the number of larvae taken in a collection of ten dips of surface water, the dips being made with an ordinary white enameled water dipper having a diameter of about five inches. At the time of each collection the environmental conditions obtaining in the area and the hydrogen-ion concentration of the surface water were recorded. A sample of the top half-inch of water was then taken and carried immediately to the laboratory. After thorough shaking, one cubic centimeter was placed in a counting cell and a count was made of the number and kinds of organisms occurring in 40 cu. mm. of water as a basis for computing the rate of occurrence of the organisms per c. c. in the breeding water.

Determinations were made of the forms as far as genera whenever possible, but those not readily fitting into the keys available were grouped only into classes. The Anopheles larvae collected were also taken to the laboratory, determined as to species, and dissections made of some (usually five) of the larger specimens in order to ascertain the nature of the food ingested. In only two instances were species other than *quadrimaculatus* found, and these were taken from areas where *quadrimaculatus* also occurred. In these two cases the gut contents for all species were similar.

EFFECT OF TEMPERATURE, PRECIPITATION, AND QUANTITY OF SURFACE WATER UPON LARVAL RATES

The records of the observations were summarized in various ways. In comparing larval rates with temperature, precipitation, and the quantity of surface water present by months, it was found that during 1928 the larval rate rose and fell with the rise and fall of the mean temperature, the highest rate coming in August, when the mean temperature (82.3° F.) was highest. In the following year, however, there were two peaks in the larval rate, one in May and the other in September, in which months the lowest mean temperatures occurred (72.2 and 75.8° F., respectively). It has always been the writer's experience in this locality that the variation in summer temperatures does not noticeably affect larval population as measured by dipping.

The summer rainfall in this region is not usually sufficient to keep the water areas from showing a steady decrease as the season advances. This gradual decrease tends to keep the margins of the water areas free from vegetation, which encroaches on the shore line in times of stationary or rising water, and to remove from the surface of the water large quantities of floatage which are blown to the margins and stranded by the wind. Except in the case of heavy rains, this material is not refloated until the high waters of the ensuing winter return. The lowering of the water level also leaves the tree and brush covered marginal areas dry, particularly in the lakes, and in those lakes, the central parts of which are devoid of aquatic vegetation, Anopheles production ceases.

During 1928 the surface water decreased very slowly from May to August, large quantities of debris and

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†Bureau of Entomology, United States Department of Agriculture.

vegetation remained on the water surface, and conditions were more or less stable in the breeding areas. During this period the larval rate showed a gradual increase. A rapid drying of the surface water then occurred from August to September, and this stranded the debris and vegetation and caused a decline in the larval rate. In 1929 the surface water decreased rapidly from May to August, as did the larval abundance. From August to September, however, there was little decrease in the surface water, making for a more stable condition in the breeding areas, which was accompanied by a rise in the larval rate.

It must be emphasized that the effects of seasonal conditions on Anopheles abundance here given are as they occurred under environmental conditions existing in this region during the two years under consideration. Under different conditions a lowering water level may increase larval abundance by making large, central, open areas in shallow lakes suitable for Anopheles breeding. One example may be cited of a large lake in which the early spring breeding was entirely marginal. The bed of this lake was covered by a rather thick growth of Potamogeton and Chara which early in the season did not reach the surface. As the water became shallow the stems and leaves of these plants came to lie at the water surface, providing excellent protection for larvae and giving rise to intensive breeding over hundreds of acres of water surface.

SEASONAL VARIATION IN ABUNDANCE OF PLANKTON

There was a wide variation in the abundance of plankton organisms in the water during the season, but their number seemed to increase as the season advanced and as the water decreased. This increase was, however, very irregular and was caused no doubt by the common phenomenon of periodicity in certain species of organisms.

COMPARISON OF LARVAL RATES AND PLANKTON COUNTS

A comparison of organism counts for the two seasons under consideration with larval abundance, irrespective of environmental conditions in the water areas, indicated a general tendency for the nonbreeding waters to have a higher plankton content than the breeding waters, and also for those breeding areas having the highest larval rates to have the lowest plankton rates. This was found to be true whether the total plankton or a major class of organisms was considered. However, in comparing the plankton abundance in those areas having larval rates up to ten per ten dips with those having greater rates, it was shown that there was really little difference in the average plankton abundance in the two groups.

The greater abundance of plankton organisms in the nonbreeding stations can be ascribed to the fact that these stations are usually those in which the water is unshaded or has no aquatic vegetation or debris covering the surface. This condition favors more rapid growth and multiplication of chlorophyll-containing organisms than occurs in the shaded or partly shaded areas in which most of the Anopheles breeding hereabout takes place.

FACTORS IN LARVAL PROTECTION

The fact that the waters of this locality are well stocked with the top water minnow (*Gambusia affinis* Raf.) makes it necessary that protection of some nature be afforded Anopheles larvae before development can take place. This condition has been demonstrated by clearing and impounding projects in the vicinity which have eliminated Anopheles breeding. Although other factors in addition to lack of vegetation and debris for larval protection may be involved in bringing about this condition in cleared and impounded areas generally, it is certain that unless protected from their enemies Anopheles larvae do not develop in numbers in this vicinity.

Protection to larvae is afforded in waters in their natural state by floating vegetable debris and by plants which grow in or at the surface of the water in such a manner as to conceal the larvae from their enemies. Floating debris can be divided into two classes: large debris and small debris. The former consists of logs, fallen trees, sticks, leaves, and so on, which do not tend to form a compact mass on the water surface, and do not give very effective protection to the larvae. The latter is composed of small particles of rotting vegetable matter resembling coarse sawdust, which collect on the water surface to form mats of various sizes, and in which the larvae are well protected against their enemies. Floating debris is much affected by wind and by the rising and falling water levels caused by alternating periods of rain and drought. In open areas and in the absence of vegetation or large debris to serve as anchorage, a wind will sweep the smaller material to shore, where a lowering water level will shortly strand it until a later rain causes the water to rise. In this manner good larval protection may be alternately present and absent in the same location. The same process is in effect with the larger material, but to a lesser extent, as this material, especially the fallen trees and logs, tends to become anchored.

Of the plants which serve as protection for Anopheles larvae, perhaps the most important are the filamentous algae which grow at or just below the surface film of the water. Anopheles larvae usually thrive in their presence. Ceratophyllum, Potamogeton, Chara, and others of the larger plants which grow in the water, and parts of which come to lie at the water surface, provide protection in essentially the same manner as the algae. Floating plants, such as Lemna, Heterantheria, Wolffia, Azolla, cannot be considered effective protection for Anopheles larvae on account of the fact that their leaves lie on top of the water surface and therefore do not effectively hide the larvae. Patches of such plants, however, when not too dense, usually harbor attached

algae or other materials which favor mosquito breeding. Reference is frequently seen in literature to the deterrent influence of these surface-covering plants on mosquito production, and the writer's observations showed that when they form a complete surface mat Anopheles breeding is absent. However, this condition is seldom met with, and when these plants occur in lesser abundance accompanying conditions are such that good mosquito breeding territory is usually indicated.

Plants such as Castalia, Nelumbo, Saururus and some grasses, which root on the bottom and extend to or through the water surface, while not of themselves providing much protection, serve as attachment and lodging places for protective materials such as algae and debris.

Plants which have large root and stem masses below the water surface and which send shoots above the water, sometimes in such profusion as to hide the water surface entirely, may or may not indicate good larval breeding areas. In this class are such plants as Jussiaea, knotweed, smartweed and hempweed. Jussiaea, for instance, by the nature of its growth seems to offer excellent protection for larvae, and when only small growths of it are present in an area larvae of all sizes are likely to be found among its algae-coated stems and roots. However, when an area becomes thickly covered with this material, even though conditions in spots appear favorable, Anopheles breeding is often very spare or lacking. While this plant grows luxuriantly under a variety of conditions, it shows a particular tendency to grow rapidly and to form a dense covering over the water surface in newly cleared and impounded areas. For some reason, this luxuriant growth has not often been observed to persist in the same location for several successive years.

ADAPTABILITY OF LARVAE

Our common Anopheles mosquitoes are undoubtedly very adaptable to a wide variety of breeding places, and lacking their preferred habitat, they may readily choose another. Because larvae are not found in a certain location, therefore, there is no reason for believing that conditions in that area are such that they cannot develop there. For example, in the course of airplane dusting operations a few years ago, it was found that only the shrub and Nelumbo covered marginal areas in a large lake were breeding Anopheles, no larvae being found in the large central area of the lake, which was covered with growths of the white water lily (*Castalia odorata*). Both areas had a thick subsurface growth of Ceratophyllum, Potamogeton, Utricularia and algae, supplying excellent protection for larvae. A period of drought caused the marginal areas to become dry, after which intensive breeding occurred all over the Castalia-covered area.

EFFECT OF ENVIRONMENT ON LARVAL RATE

The records on the rates of occurrence of Anopheles larvae in the various environments showed that in places where there was no small debris the larval rates were highest where green filamentous algae occurred, either alone or mixed with blue-green algae. When blue-green algae occurred alone, however, the larvae were rather scarce, indicating that Anopheles mosquitoes avoid these areas to some extent. Areas without filamentous algae of any kind, but in which weeds and grass occurred, gave substantial breeding rates, while very low rates were found where large debris offered the only protection.

In areas in which small debris was present, which material has been previously mentioned as being effective protection for Anopheles larvae, the differences in the breeding rates occurring when algae were present or absent were less noticeable. In both 1928 and 1929, however, the areas having a general mixture of debris—grass, algae (both green and blue-green), and weeds—showed the highest breeding rates. The deterrent influence of blue-green algae on larval abundance when occurring without green algae was also indicated.

RELATION BETWEEN LARVAL RATE AND PLANKTON ABUNDANCE

The counts of food organisms present in all these waters showed an abundance of available food for the larvae and a tendency for the areas with the highest breeding rates to have the lowest plankton rates, a point which has been discussed previously.

In comparing the rates of occurrence per c. c. of the more common plankton genera with the absence of Anopheles larvae and their presence in increasing numbers, no definite trends were found; that is, the quality of the plankton in the nonbreeding and in the breeding areas having low larval rates was not essentially different from that in those areas having high larval rates.

HYDROGEN-ION CONCENTRATION OF BREEDING AND NONBREEDING WATERS

The record of the hydrogen-ion concentration showed both breeding and nonbreeding waters to be predominantly alkaline in reaction and to about the same degree. Most of the readings in open impounded areas where no breeding occurred were, however, somewhat higher than those in the breeding areas, being 8.01 as against 7.42.

RESULTS OF LARVAL DISSECTION STUDIES

The results of the larval dissection studies showed that there was considerable variation among the various organisms in the percentage of times they were found in the larval gut when present in the breeding waters, but they indicated that most of the genera, whether those commonly or those rarely present in the breeding waters, are liable to ingestion by the larvae. Whether this is by choice or chance is problematical. The amount of maceration undergone by the different organisms while in the mouth of a larva and their varying degrees of digestibility undoubtedly have a great influence on the condition of the material when found

in the larval gut, and consequently on the chance of their being recognized. Observations under the microscope of larvae in the act of feeding revealed no selection of food particles. The larvae ingested whatever was presented, provided that it was of suitable size. The larvae used two methods of feeding upon filamentous algae. At times they ingested the entire filament and at other times they ran a filament between the mandibles, chewing and sucking out the cell contents as it went through the mouth, and then discarding the empty filament. Any material subjected to the latter treatment would of course be impossible to identify and there would be no record of its incidence in gut examinations. It is believed that the difference in character of available food materials, rather than any selection by the larvae, accounts in part for the fact that some organisms are recognized in the gut more often than others which are apparently as available and as suitable for food. Also in the work here summarized the determination of organisms present in the breeding water was made from samples of the top half-inch of water, and there were undoubtedly included certain organisms whose preferred habitat was below that in which Anopheles feeding principally occurs, so that they appeared only occasionally in the larval examinations.

SUMMARY

During the summer months of 1928 and 1929 observations were made on various environmental conditions obtaining in Anopheles breeding and nonbreeding waters in northeastern Louisiana to determine, if possible, those factors which are concerned with the varying degrees of abundance or with the absence of larvae.

As measured by the numbers occurring in collections of ten dips of surface water, the abundance of larvae in the breeding areas was not greatly affected by variations in the mean summer air temperature, which in each month was above 70° F.

Protection for larvae is necessary in the water areas studied on account of the presence in abundance of the top water minnow (*Gambusia affinis*) and other natural enemies. This is provided in the breeding areas by floating vegetable debris and by various species of plants, the best protection being afforded by small floating debris and by filamentous algae. Water areas containing filamentous blue-green algae in the absence of green algae were not found to be very favorable for Anopheles larvae. In areas completely covered by Lemna, Anopheles larvae are scarce or lacking, but lesser amounts of this material usually indicate breeding areas. Under certain conditions a rapid decrease in surface water was found to decrease larval incidence as a result of the stranding of protective materials.

The plankton content of the breeding and nonbreeding waters was computed on the basis of the occurrence of the various groups of organisms per c. c. of surface water. It was found that as a rule larger numbers of plankton organisms occurred in the nonbreeding waters, and this was explained in part by the fact that the breeding waters usually are more shaded and the surface is covered to a greater extent by vegetation and debris, a condition which causes the development of fewer chlorophyll-bearing organisms. The character of the plankton as regards composition by classes of organisms in the different locations varied considerably, but no consistent differences between breeding and nonbreeding waters were found.

The range of the hydrogen-ion concentration in the breeding and nonbreeding waters was found to be essentially the same, and all waters were principally alkaline in reaction.

Examination of the gut contents of larvae showed that any organisms of suitable size are likely to be ingested when present in the water, but that some available forms are recognized in the gut less frequently than others. This may happen because the preferred habitat of certain organisms does not coincide with that in which larval feeding chiefly occurs, or on account of the varying degrees of maceration undergone by different organisms when they are eaten by the larvae.

DISCUSSION (*Abstract*)

Dr. T. H. D. Griffitts, Albany, Ga.—We have had, at different times, more or less learned papers on the subject of the breeding of Anopheles in certain vegetation. A few years ago a paper was published indicating or suggesting that malaria had been driven out of the City of New Orleans by means of the water hyacinths which occupied bodies of water in the City. To examine bodies of water in one locality and conclude that Anopheles do not breed there because they are not found there may be entirely misleading. In many sections water hyacinths furnish the normal home for *Anopheles quadrimaculatus*. The same holds true with other classes of vegetation. Too frequently we are inclined to classify areas in certain locations as *quadrimaculatus* breeding grounds simply because of the fact that they are found there at a particular time. In attempting to find *Anopheles atropos*, a certain Anopheles that produces in salt water, to study its ability to transmit malaria, I examined a certain salt pool in a marsh (by the way, Dr. Mohr, in your County of Mobile) which had been classed as an *atropos* breeder. With high tides it filled with sea-water and produced A. atropos. Filled with rain water from continued heavy rains, this pool produced *quadrimaculatus*.

Mr. Bradley (closing).—I have recently been transferred to Florida and have found conditions there much like those in Louisiana. Some places breed Anopheles continuously, others only from time to time. Not always, but often, this latter condition is associated with environmental changes.

ANALYSIS OF REPORTS OF 8,354 CASES OF IMPF-MALARIA*

By WILLIAM KRAUSS, M.D.,
Bolivar, Tenn.

The term, "impf-malaria," not used in America, has the merit of brevity and of being unequivocally descriptive. *Impen,* to vaccinate, distinguishes from Anopheles malaria.

American writers on the subject of malariatherapy are saying very little about malaria, the disease, as modified by the "impf" method on the one hand, and the pathological individual, the paretic, on the other. In England and on the Continent malariologists have contributed much to the literature of induced malaria, and the fatalities have been very much less than in this country. Malaria is a disease in which the chief injury lies in the reticulo-endothelial system, which, in paretics, has been taxed to the utmost. It has been held by Muehlens[14] and Bruetsch[15] that the reaction of the endothelial cells is an important element of the cure.

Although perhaps more than 20,000 patients have been treated by this method, many are deterred from using it on account of the high mortalities reported and for other reasons. In a not inconsiderable experience extending over many years, I do not recall ever having had a death from tertian (vivax) malaria. While connected with the medical school in Memphis I had occasion to make daily blood examinations on a few cases being treated with impf-malaria for general paralysis. Since I have been at this institution I have followed the same practice. Obviously we cannot ascribe a death to malaria unless we know how heavy an infection we have permitted to develop. Without this precaution it is also quite possible to permit a spontaneous intercurrent subtertian infection to be transferred to a recipient. I have undertaken, by means of a questionnaire, to get data upon which a discussion could be based. The detailed data of this questionnaire will be discussed *seriatim* under the respective heads.

QUESTIONNAIRE

(I) GENERAL INFORMATION

(1) Number of patients treated?
(2) Number of malaria deaths?
(3) Method of inoculation?
  a. Percentage of "takes."
  b. Seasonal influence.
  N. B.—If more than one method, which has been most successful?
(4) Percentage of spontaneous termination of malaria?
(5) Average duration, or number of paroxysms?
(6) Method, if any, for reducing severity of malaria?
(7) Method, if any, to prevent spread?
(8) Percentage of malarial relapses or "chronic" malaria?

(II) AS TO FATAL CASES

(1) Ages of patients?
(2) Sex of patients?
(3) Physical condition (treatment risk).
(4) Season of year?
(5) Authenticity of strain (pure vivax).
(6) Number of paroxysms before death?
(7) Ratio of parasites to r. b. c. before death?
(8) What premonitory symptoms of fatal issue?
  (a) Anticipation of paroxysms.
  (b) Duplication or diffusion (quotidian or prolonged paroxysms).
  (c) Hyperpyrexia.
  (d) Rapid increase of parasites.
  (e) Rapid fall of hemoglobin.
  (f) Albuminuria.
  (g) Bilious vomiting.
  (h) Other.

The material for this study is taken from 52 reports from 68 institutions in 24 states. Other material was obtained from institutions which were not using malaria. No reports were received from sixteen states. Some institutions had abandoned the use of malaria because of difficulty in keeping strains going, some because of too many negative inoculations (especially in negroes), some because they consider malaria treatment too dangerous. Some referred malaria treatment to sister institutions which were thoroughly organized for carrying out this treatment. Others used other thermogenic agents which the Vienna school reserves for malaria-refractive cases; others have abandoned malaria therapy for diathermy.

Some of the data offered in reports appear to be mere approximation. Also, in some instances statements like "Nearly all," "Not many," "Very few," taken from letters and reprints sent in lieu of categorical answers, had to be translated into arbitrary figures to permit tabulation. On the whole, the data collected are reasonably accurate and complete. Upon careful digestion of analyses given in the accompanying letters and reprints, I believe that it is safe to offer the figures as giving a fair cross-section of the situation.

It is proper at this place to express my heartfelt appreciation of the wholehearted cooperation received. Thanks are also due in no small measure to our Superintendent, Dr. E. W. Cocke, who, although mainly interested in diathermy, has placed all his patients at my disposal; also, to our Clinical Director, Dr. H. M. Francisco, for expert advice and assistance, as well as to the whole clinical staff.

Table 1

DEATH RATES

	No. Reporting	Cases	Deaths	Per Ct.	High	Low
Unselected cases	22	3565	338	9.02	24.63	2.2
Selected cases	19	3539	45	1.02	5.86	0
Not stated	11	1265	65	5.14	9.00	0
Totals	52	8354	448	5.38	24.63	2.2

These figures for selected and unselected cases are nearly even, but the death rates, 9.02 and 1.02, respectively, have a ratio of 9:1.

*Read before National Malaria Committee (Conference on Malaria), meeting conjointly with Southern Medical Association, Twenty-Fifth Annual Meeting, New Orleans, Louisiana, November 18-20, 1931.

*From the Western State Hospital.

COMMENT

Some physicians do not accept patients for malaria treatment unless their general condition is good and there are no contraindications. Others accept all cases for treatment, but place them under trained supervision, which is the policy followed at the Vienna school.* There must be a wide latitude of opinion as to what would be called a good or bad risk. Doubt is expressed by some as to what is properly a malaria death. The most significant fact which emerges from this inquiry is that those who report several series of cases are having better results in their later series. In one report it is stated that "we now have no deaths that can be strictly ascribed to malaria." The modes of death and premonitory symptoms will be discussed below. There must be cases in which the cause of death may be indeterminable without an autopsy by a malaria expert.

We inoculated fourteen negroes without a single "take." One old negro had a fatal convulsion seven days after inoculation. Parasites had never been found by the thick film method. Such a death after one or two chills might easily be ascribed to malaria.

An attempt was made to ascertain a climatic influence. Institutions were grouped as "Eastern," "Middle West," "Pacific," "Southern." In the Middle West group some were in malaria territory.

Table 2

REGIONAL DISTRIBUTION

	No. Reporting	Cases	Deaths	Per Ct.	High	Low
Eastern group	23	4272	314	7.35	24.63	0
Midwestern group	18	2746	74*	2.73	5.88	0
Pacific group	5	994	46	4.62	8.62	2.2
Southern group	5*	228	4	1.79	11.00	0

*Figures approximate.
*One Southern excluded; includes all general paresis deaths.

This table will be analyzed under "Discussion."

In answer to the question, "How many successful inoculations?" we get the following data:

Table 3

PERCENTAGE OF SUCCESSFUL INOCULATIONS

	No. Inst.	Cases	Per Ct.	Total Inoc.	High	Low	Negroes
Eastern group	17	2675	87.70	3049	100	70	10-40%
Midw't'n group	10	1179	96.55	1220	95	82	Few*
Pacific group	5	994	87.59	1135	97	75	No R.
Southern group	4	196	79.03	248	88	60	Few†
Totals	36	5038	89.13‡	5652			

*Comments: "less," "none," "few," "discontinued trying."
†One, all negative.
‡Reporters do not specify in all cases if gross percentages include negroes.
Eastern group includes 10, 25, 40, 60 per cent successful in negroes.
The total inoculations are calculated from the percentages given.

It is pertinent here to quote Barber, Komp and Hayne,[1] who collected data on the incidence of benign tertian and total malaria in the Mississippi Delta in all months as follows:

Total positive slides, whites 2079, benign tertian, 51.3 per cent
Total positive slides, colored 2446, benign tertian, 16.5 per cent

This is a ratio of more than three to one. Add to this the fact that the whites live a more sheltered life and are less exposed to infection. Thonnard-Neumann[2] administered 5 to 8 c. c. of blood containing subtertian parasites to six West Indian negroes who were suffering from disease of the nervous system. In four cases the malaria ran without fever, in two cases it lasted only two to three days, in all but one the parasites tended to disappear spontaneously. When one considers the extreme virulence of subtertian malaria in paretics, this is indeed surprising. On the other hand, it is reported that negroes are poor treatment risks.

Table 4

SPONTANEOUS TERMINATIONS OF MALARIA

	No. Inst.	Cases	Spont. Term.	Per Ct.	High-Low	Negro
Eastern group	17	3204	374	11.67	0-30	10, 50%
Midwestern group	18	1249	128	10.24	0-25	?
Pacific group	4	893	340*	?	30-70	?
Southern group	4	173	43	24.85	11-80	Very many
Totals	43	5519	885	15*	0-80	

*Estimated from approximate answer.

What influence has the method of inoculation and the dose of the injection? Answers to these questions do not lend themselves to tabulation. *A priori* it is assumed that massive intravenous injections into compatible individuals would produce a high percentage of "takes" and have a short period of incubation. Not a single reporter or writer consulted speaks of the influence of a rich infection. Of course, it is known that even when no plasmodia are found, the blood may still be infectious. Most writers object to too long a period of incubation. In this age of speed this is an important objection. On the other hand, injections of large quantities of blood intravenously, giving an actual continuation of the fever in the recipient without a period of incubation, throws down the patient rather hard. This, of course, is not "tertian malaria." Hecht-Eleda[3] notes, as all others have done, that in cases of general paralysis injected with benign tertian blood, the fever generally runs a quotidian course. On the other hand, of syphilitics in various stages other than general paralysis, 285 cases were injected intravenously with 3 to 5 c. c. of tertian blood. Two hundred and forty-seven ran a typical tertian course, the highest point being fairly constant, between 40 and 41° C. (104-105.8° F.). The greater frequency of the tertian type of fever in these cases as compared with that in general paralysis is, in the opinion of the author, largely due to the difference in the condition of the patient.

The British malariologists,[4 5] infecting with mosquitoes, call attention to the atypical character of first

*Except in galloping paralysis.

reactions to the infection. The fever steadies down to the tertian type, but later, after further increase of parasites, the paroxysms tend to become quotidian.

As to the stage in the cycle of the parasites, or the number of chills permitted before using the patient as a donor, experiences vary greatly. Generally speaking, good results have been shown under all conditions of transfer, but they have been best when a direct transfer was made. Many experiments made abroad for determining the best treatment of blood for shipping show that malaria blood may be infective after seventy-two hours if refrigerated. As good a plan as any is to defibrinate with glass beads in a sterile vessel and transfer aseptically to the tube in which it is to be shipped. Hemolysis is no bar to results. Soon after any method of treatment the parasites escape from the blood corpuscles and assume a spherical, gametoid form, which, however, is no disadvantage.

In the Western State Hospital (Tennessee) we await several chills, determine the ratio of parasites to cells and inject intracutaneously. If the ratio is very low, we use more blood or inject in two ways. The number of c. c. injected is no measure of the amount of malaria. If the first injection is negative we have the experience of greater resistance and proceed accordingly.

The answers to the questions as to the number of paroxysms allowed run to a rather high figure, averaging perhaps fifteen. Individual reports run as high as thirty-two or "as many as they will have." This will be commented upon later.

No seasonal influence upon successful inoculations is admitted.

No successful method of reducing impf-malaria to a tertian periodicity has as yet been developed.

With respect to screening, it is generally assumed that the strain used is asexual. No transmission has been noticed, according to reports.

Relapses appear to be extremely uncommon. This is in striking contrast with the experience of the British, using Anopheles malaria.

The second part of my questionnaire, "As to Fatal Cases," included questions as to age, sex, physical risk, season of the year, none of which was believed to have any bearing except extreme age. Two report more deaths in hot weather. The authenticity of the strain was generally assumed to be satisfactory. The chances are that an accidental introduction of *P. falciparum* infection would have declared itself at once by heavy fatalities. Some appear to have had no apprehension with respect to the possibility of an intercurrent subtertian infection, being satisfied that because the strain was received from a particular source there was no occasion for any concern.

The number of paroxysms before death varied greatly. Some died after the first, second or third chill. One rupture of the spleen after five days of apyrexia must have been due to direct violence. Another ruptured spleen occurred after the third chill. No one will doubt that these were malarial deaths.

Under "premonitory symptoms of a fatal issue," under the questions, anticipation, duplication or diffusion of paroxysms, hyperpyrexia, rapid increase of parasites, rapid fall of hemoglobin, albuminuria, bilious vomiting, the usual answer was "no data." The causes mentioned most often were circulatory collapse and convulsions. Other causes of death given were hyperpyrexia (three), albuminuria (two), vomiting, gastrointestinal disturbance (three), hemorrhage (one).

DISCUSSION

Table 1 shows a wide variation in the fatalities, especially as between selected and unselected groups. If the careful selection of cases is an expression of caution, the inference follows that these reporters also subject their cases to very careful supervision and management. After all, malaria is not a drug but an infectious disease and cases should be under the care of someone who understands malaria, and should have the benefit of consultation with an expert malariologist. There should be repeated checkings of the laboratory work, especially of the staining. Except in the South and in teaching institutions very few are competent to examine for malaria. This important detail seems to be generally neglected.

As to selection of cases for the sake of better mortality, patients should not be deprived of the benefits of the treatment, as surprising results have followed the treatment of desperate cases. Extreme weakness and galloping paralysis are positive contraindications.

Regional influence upon death rate, percentage of successful inoculations and spontaneous termination may be discussed together. The influence upon death rate is complicated by difference in selection of cases in the central group and by the fact that in some large Eastern institutions the work was begun when the effect of paresis upon the course of a tertian malaria was not sufficiently appreciated. There is also the factor of large doses and greater number of paroxysms in this group. These data balance better in the other three groups.

In the South, in three institutions, there were 192 cases with 2 deaths, 27 cases with no deaths, and 67 inoculations without a death.

As to the other data, there is unmistakable evidence of climatic influence and resistance of residents in malarious districts. Some Southern institutions report that they have discontinued malaria treatment altogether because of refractoriness to inoculation, spontaneous terminations and apyretic course of the malaria. Three of our strains have died out in one season. In one series of six injections there was not a single "take." The Pacific group may claim "climate," as there seems to be no other answer.

The negro rate has been discussed. We expect to experiment with diathermy in refractory cases.

The mode of injection and size of the dose doubtless influence the severity of the reactions. Massive injections of heavily infected blood into compatible patients may result in dangerous reactions. The quotidian char-

acter of malaria in paretics is evidence of lost resistance. The reticulo-endothelial system has been heavily taxed. The Vienna school[6 7] prefers the extravenous route because of the longer period of incubation. It cautions against frantic attempts to overwhelm patients with heavy infections, preferring to reinoculate with another strain or eventually try other pyretogenic methods (such as living sensitized typhoid bacilli). Ebaugh,[8] Bahr,[9] White,[10] and others use this method by preference and also record a very low death rate. This method permits the adjustment of the body to the infection, and the tertian type permits a partial unloading of the splanchnic circulation. I have a feeling that digitalis is not without danger. I would prefer "diffusible stimulants."

Williams[11] states that the effect of injected malaria (in paretics?) on liver function is marked. He prefers the levulose tolerance test to the van den Bergh for the study of function.

It has been stated that malaria too soon after arsenicals fails to "take."

Should mosquitoes be used to bring down refractory cases? The propagation and preservation of mosquitoes after infection can succeed only in the hands of specialists with long training. The shipping presents no difficulties, nor need there be any apprehension that they might escape. All this is a matter of technical detail. British writers have thoroughly tested out all the possibilities of the "natural" method of inoculation. Patients have been refractory to this method also, but where the other method has failed it may nevertheless succeed. The period of incubation is more normal, the periodicity more likely to be typical, although even here the quotidian type of fever occurs often. Anopheles malaria is more refractory to quinine; the tendency to recrudescence and relapse is great. The inevitable production of gametes introduces the danger of dissemination, especially in the South, where failures by the blood method are common. Nevertheless, it would be very desirable if the United States Public Health Service could maintain one depot, so that institutions might start their malaria with one or more authentic strains. Malaria has been successfully transmitted by expressing sporozoites from salivary glands into serum and immediately injecting. Unfortunately these cannot be shipped. At least no attempt has been successful. Southern institutions could confine their transmissions to the winter months and early spring and make a thick-film check of the blood in the spring.*

The influence on death rate of keeping up the infection too long must be considered. Those who formerly permitted eighteen to twenty-four paroxysms or "as many as they will have" showed the highest death rate in the period just after the malaria. The extreme emaciation, weakness and blood destruction following prolonged treatment not only defeat the object of the treatment, but endanger life. It is better to terminate the infection if the patient does not react well between paroxysms, and to inoculate again later.

The discussion of causes of death involves many factors. We have to deal with a seriously damaged patient, whose symptoms, especially in the meningovascular type of the disease, may become suddenly aggravated. Any existing cardiovascular damage has to be considered. We should not record a death as due to malaria unless a high degree of infection is noted upon examining a blood smear. In the introduction this has been mentioned. As yet I have not seen a death from malaria in a paretic.

With respect to convulsions, many consider a history of convulsions a positive contraindication for malaria treatment. The comment here is in order that this should apply as well to other forms of pyrexia, since this is a manifestation of pyrexia rather than of malaria. But convulsions have occurred in the course of malaria in patients who have no history of seizures prior to admission. Bunker and Kirby[13] say:

"* * * * convulsions seem to lie outside of the sphere of coincidences. * * * * * five of our general paralysis patients (had) * * * * * typical seizures, the most recent convulsions having occurred nine days, forty-eight days, fifty-nine days, seventeen months and twenty-seven months prior to inoculation."

All had some convulsions during the course of the malaria. Three of them died, but the other two had no further seizures. On the other hand, two without any history developed them during or after the malaria. This excerpt is typical of comments concerning convulsions. If possible, premonitory symptoms should be controlled.

The cardiac collapse and the rare cases of ruptured spleen are due primarily to splanchnic congestion. Whiskey is a better drug than digitalis for meeting this indication. Death is often a matter of minutes. The patient should be given an intravenous injection of glucose and caffein sodio-benzoate. Mere low blood pressure is a symptom of malaria to be expected during intermission. Gastrointestinal symptoms are danger signals in malaria. The function of the kidneys, and especially the output of urea should be watched. In the absence of facilities for perfect blood work, the hemoglobin should be estimated frequently.

SUMMARY

A study of reports from mental institutions using impf-malaria has been presented.

The primary object of the study was to determine, if possible, the reason for high death rates.

A tabulation is presented giving gross rates, rates according to selection of treatment risks, regional distribution, per cent of positive inoculations and conditions influencing them, per cent of spontaneous terminations, season of the year in which failure occurred, number of paroxysms permitted, precautions taken to prevent spread, means employed for reducing the severity and frequency of paroxysms, and possibility of relapses.

*I am not unmindful of the fact that winter infection may have a very long period of incubation.

In the fatal group, the relation of age, sex, season, physical risk, authenticity of strain and number of paroxysms permitted, to death rate, was sought.

Prompt recognition of premonitory symptoms is urged.

The possibility of an accidental intercurrent estivo-autumnal malaria is suggested.

The desirability of a daily check upon numerical increase of parasites is presented.

The epidemiological side of malaria inoculation is considered.

The possible influence of massive intravenous infection and of too prolonged a course of malaria upon death rate is detailed.

The importance of perfect hospital organization and a better understanding of malaria as a disease is urged. Some of the symptoms of fatal cases are discussed.

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DISCUSSION (*Abstract*)

Dr. W. K. Stratman-Thomas, Chattahoochee, Fla.—One can understand some of the difficulties encountered by Dr. Krauss in his evaluation of material from many different sources. Reliable data cannot be secured unless the case in question has been followed daily by a physician acquainted with the clinical course and laboratory findings of malaria. At the Florida State Hospital, where malaria therapy has occasioned no harmful effects, all patients admitted to treatment undergo a rigid examination which excludes all but young and robust individuals. The clinical course and laboratory findings are followed daily. Routine inoculation of paretics at this institution is effected by the utilization of anophelines harboring *P. vivax*, supplied through the kindness of Dr. Mark F. Boyd, Director of the Station for Malaria Research, Florida State Board of Health, Tallahassee. In our hands benign tertian malaria induced by application of anophelines has responded as readily to quinine as a *P. vivax* infection obtained by blood inoculation. The existence of "gametocyte-free" strains is still to be demonstrated. Unscreened wards are potential foci of malarial infection and the suggestion is not untenable that malaria therapy may be partly responsible for sporadic outbreaks of malaria in Northern states. It is recommended that the discharge of all patients who have received malaria therapy be reported to the proper health authorities as is done in England.

Addendum: Since this paper was presented I have been able to carry on parallel series of impf. and Anopheles-malaria, thanks to the courtesy of Drs. Boyd and Stratman-Thomas.

A REVIEW OF RECENT CONTRIBUTIONS ON THE TREATMENT OF MALARIA*

By CHAS. F. CRAIG,
M.D., M.A. (Hon.), F.A.C.S., F.A.C.P.,†
New Orleans, La.

(b) *Treatment.*—Most of the literature during the period under review has dealt with the relative value of quinine and plasmochin in the treatment of malarial infections. Bass[78] (1930) states that he considers that the cinchona alkaloids, especially quinine, are our only specific remedies for malaria. While he admits that therapeutic results can be obtained with the arsenicals, plasmochin and other quinine substitutes, he does not believe that their use should replace quinine or that the results obtained, because of the toxicity of these drugs, are worth the price paid.

Sinton[79] (1931) concludes that the number of permanent cures produced by quinine is increased by prolonged courses of treatment, and that such cures follow the administration of larger rather than smaller doses of the drug. He recommends thirty grains of quinine a day for one week for the treatment of all primary malarial infections, and that precautions should be taken to see that the drug is absorbed. He makes the following statement, which is rather surprising: "Such treatment, if properly carried out, should cure at least 70 per cent of fresh malarial infections." One cannot help but believe that the author is too optimistic, for it is very doubtful that one week's treatment

This is one section of a comprehensive paper entitled "Review of Recent Advances in Knowledge of Malaria," read before the National Malaria Committee (Conference on Malaria), meeting conjointly with Southern Medical Association, Twenty-Fifth Annual Meeting, New Orleans, Louisiana, November 18-20, 1931. The complete paper with the complete bibliography will be reprinted as a part of the Symposium on Malaria and may be obtained from the Southern Medical Association, Empire Building, Birmingham, Alabama, or from Dr. Mark F. Boyd, Secretary, National Malaria Committee, P. O. Box 793, Tallahassee Florida.

*From the Department of Tropical Medicine, School of Medicine, Tulane University, New Orleans, Louisiana.

†Colonel, U. S. Army, retired.

of even primary infections with the dosage of quinine recommended will cure such a large percentage of cases.

The question of the occurrence of quinine-fast strains of the malaria plasmodia is still attracting attention. The evidence as to the existence of such strains is, up to the present, absolutely unreliable and will not bear close analytical study. The most recent contribution to this subject is that of Sinton[80] (1931), who discusses the question of variation in virulence of different strains of the same species of plasmodium and the existence of quinine-fast strains. He instances the great diversity of opinion regarding these questions by many authorities and concludes that in the case of *Plasmodium vivax* the evidence very strongly supports the view that variations in the strain or virulence of this parasite do exist. However, he is very doubtful that quinine resistant strains exist and states that a search for such quinine-fast forms in northern India, covering near'y 4,000 cases, failed to reveal a single case in which the plasmodia were resistant to quinine.

During the past year a large number of papers have appeared in which the value of plasmochin or a combination of plasmochin and quinine is considered. Space forbids the consideration of most of these papers at this time, but that by Major Manifold[81] (1931), Royal Army Medical Corps, is probably the most important that has appeared to date. Manifold details the results of a study of the treatment with plasmochin and quinine in thirty-five hospitals under the control of the Royal Army Medical Corps in India. The same treatment was used in all and consisted of one tablet containing 0.02 gm. of plasmochin and 10 grains of quinine given morning and evening for twenty-one days. Only infections with *Plasmodium vivax* were treated.

In all, 3,187 cases completed treatment, whi'e twelve patients among British troops and fourteen among Indian troops had to stop the treatment on account of toxic symptoms. Treatment had to be temporarily stopped in 21.4 per cent of the 1,298 British troops and in 10.2 per cent of the Indian troops, but in most of these patients the toxic symptoms were said to be mild, and continued experience with the drug resulted in fewer and fewer such cases.

Epigastric pain and colic occurred in 14.4 per cent of the British patients and 7.9 per cent of the Indian. In most cases the pain was slight and disappeared after cessation of treatment for a day or two. Vomiting was very unusual and abdominal pain slight.

Cyanosis occurred in 56 of the 1,298 British (4.3 per cent) and 13 of the 1,915 Indian patients (0.67 per cent). This symptom occurred in 80 per cent of the patients on or after the seventh day of treatment, and cleared up in forty eight hours after cessation of treatment in 55 per cent and in seventy-two hours in 70 per cent of the British cases. One death was reported. Dyspnea occurred in only two cases, diarrhea in ten cases, while cardiac symptoms were negligible and not so frequent as might be expected with quinine alone. Albuminuria occurred in five cases.

Manifold concludes that the dosage of plasmochin used may be safely given to all classes of patients, provided they are kept under observation during the three weeks of treatment. He considers that the incidence of severely toxic symptoms is small and that such symptoms are of importance in only a very few patients who have a special idiosyncrasy to the drug. After a temporary cessation of the treatment for a day or two, he states that it can be continued in the great majority of cases for the required period.

The relapse rate after this method of treatment he found to be very low in patients observed for an average period of four and a half months. In such patients the relapse rate was 5.2 per cent, but if relapses were counted only after the end of the malarial season, it was only 2.4 per cent. He quotes Sinton, Smith and Pottinger[82] (1930), who obtained a relapse rate as high as 42 per cent in a series of quinine treated cases, but when they used the same treatment which Manifold used in this investigation, the relapse rate was reduced to 8 per cent. Manifold concludes with the suggestion that further work may demonstrate that good results may be obtained with much smaller doses than 0.04 gm. of plasmochin daily, and this might make it possible to issue the drug to patients not under medical supervision.

In the paper previously mentioned, Sinton, Smith and Pottinger, as a result of observations with the treatment of malaria by plasmochin and quinine, conclude that this combination is better than either drug separately, and Sinton,[83] in an excellent paper devoted to the treatment of malaria, reaches the following conclusions regarding the use of plasmochin. Plasmochin used alone is of little use in the treatment of malignant tertian malaria, has a marked action in producing both clinical and permanent cures in benign tertian malaria, but its good effects are much increased by a combination with quinine. It has a rapid destructive and sterilizing effect on gametocytes of all species of malaria plasmodia. The maximum daily dose should not exceed 0.04 gms. (about 2/3 grain) and the treatment should always be carried out under medical supervision and stopped upon the appearance of any toxic symptoms. The drug should not be given to persons suffering from lesions of the liver, kidneys or circulatory system or to weak and anemic individuals. At present our knowledge does not warrant the use of this drug on a large scale in the dosage originally recommended, but it is a very important adjuvant to quinine in the treatment of malaria, and should always be given in combination with the latter drug.

In this paper, Sinton recommends three standard treatments for malaria that are of interest and he uses two mixtures in these routine treatments. Mixture A, or the alkaline mixture, has the following composition: sodium bicarbonate, 4 gm. (60 grains); sodium citrate, 2.6 gm. (40 grains); calcium carbonate or chloride 0.2 gm. (3 grains); and water to make 28.5 c. c., or one ounce. This mixture should be well shaken be-

fore using. Mixture B, or cinchona mixture: quinine sulphate (or cinchona febrifuge) 0.65 gm. (10 grains); citric acid, 2 gm. (30 grains); magnesium sulphate, 4 gm. (60 grains); water to make 28.5 c. c. (one ounce). Of the three treatments, Treatment I is recommended in acute primary infections. After a preliminary purgation, 1 oz. of mixture A is given, repeated in one hour, and again repeated after one hour. About one-half hour after the third dose of mixture A, one ounce of mixture B is given, and one ounce of mixture A is given one half hour before every subsequent dose of mixture B.

Mixture B is given three times daily for one week, preceded each time by a dose of mixture A as directed. In addition to this, the patient receives ¼ grain (0.015 gm.) of plasmochin once daily during the week he is on the quinine treatment. This treatment, although lasting only one week, Sinton claims has a rapid action on the clinical manifestations of all three types of malaria, destroys or makes non-viable the sexual forms of all three forms of the parasite, and should permanently cure at least 80 per cent of all malignant tertian infections and probably more than 70 per cent of primary infections of benign tertian, as well as 20 or more per cent of the chronic infections. Not more than 20 to 30 per cent of benign tertian infections should relapse after this treatment.

Treatment II is used in relapsing infections, and if the relapse is due to malignant malaria, Treatment I should be repeated for one week and the quinine and alkaline treatment continued, but only twice daily, for another week with no plasmochin. If the relapse is due to benign tertian malaria, or a mixed infection, Treatment I should be repeated as for relapses of malignant tertian malaria, but the daily dose of plasmochin may be raised to 0.02 gm. (1/3 grain) during the fourteen-day course of treatment.

If a relapse occurs after this treatment due to malignant tertian malaria, Treatment II is repeated; if due to benign tertian or quartan, Treatment III is given. This consists of the administration of the quinine alkaloid dosage described in Treatment I for one week, combined with a total daily dosage of ½ to 2/3 grain (0.03-0.04 gm. of plasmochin) administered in two divided doses after meals. During the following two weeks, mixture B is given twice daily with a similar dose of plasmochin.

Sinton states that as the result of his experience with these various methods of treatment, he estimates that Treatment I should cure roughly 80 per cent of all the ordinary forms of malaria seen in general practice, irrespective of the plasmodium involved. Treatment II should cure another 10 per cent of the total, leaving about 9 per cent of chronic benign tertian or quartan and about 1 per cent of malignant tertian, of which practically all the latter should be cured by repeated treatments. Treatment III was designed to cure the remaining chronic benign tertian and quartan infections.

Although numerous other papers have appeared upon the efficiency of plasmochin in the treatment of malaria, the consensus of opinion appears to be that this drug is useful in combination with quinine, but that its administration must be carefully guarded owing to the frequency of toxic symptoms. It appears to be of great value in the destruction of gametocytes of all three species of plasmodia and those who have used it most extensively are unanimous in the statement that the relapse rate in all forms of malaria is greatly reduced where it is used in combination with quinine.

One of the great difficulties attending the treatment of malaria with quinine is the uncertainty as to whether the drug as administered is being absorbed. Even though it may be detected in the urine by easily applied tests, this does not prove that enough of the drug has been absorbed to cause the destruction of the plasmodia. Vedder and Masen[84] (1931) describe two new methods of practical value in the determination of the amount of quinine in the blood and give the results they obtained by the application of these methods. The methods can be used as a guide to the amount of quinine to be administered in the treatment of malaria by demonstrating the concentration of the drug in the blood. They found that the concentration of quinine in the blood depends upon individual variations, as after the oral administration of 10 grains one individual may have only 2 mg. per liter in the blood and another 5 mg. per liter. The authors regard these variations as the probable reason why a standard treatment will cure one individual, while another will relapse. One patient is cited, suffering a tertian relapse, who after the administration of 30 grains of quinine in three 10-grain doses showed as the highest concentration obtained on the second day 4.6 mg. per liter with no symptoms of cinchonism. The same patient when placed upon 40 grains of quinine a day developed a concentration in the blood of 75. mg. per liter, at which time he had severe ringing in the ears. The authors believe that the standard treatment of 30 grains daily would never cure this patient owing to lack of sufficient concentration of the drug in his blood. Their observations appeared to demonstrate that the administration of quinine by mouth is the best method and that there is no excuse for intramuscular injections, which are more slowly absorbed and produce tissue necrosis.

Knowles, Senior-White and Das Gupta[85] (1930) recommend the Bass method of cultivation of malaria plasmodia in determining whether parasites are present in the blood after treatment. In four cases where daily blood films had become negative, cultures showed parasites still present, and in one instance a positive culture was obtained in a patient who had received 140 grains of quinine in solution in 7 days. They recommend the use of this method in the determination of a cure.

A most useful method of preserving malaria plasmodia when it is desired to transmit these parasites through the mail for the purpose of treating paretics is described by Johns[86] (1931). The method consists in the addition to each 10 c. c. of blood of 0.2 c. c. of a 50 per cent sterile solution of dextrose, defibrinating the blood, and storing the defibrinated blood in cracked

ice. Successful infections were obtained with blood kept in this manner for as long as 18 days and such blood has been transported from New Orleans to Los Angeles, Jacksonville, Denver, Chicago, and other places and used successfully in inoculation of paretics. Johns concludes that the infectivity of this blood for eight days is fully equal to that of blood directly transferred from patient to patient.

The most important monograph upon malaria published during 1931 is that by Boyd,[87] entitled "An Introduction to Malariology," which contains most valuable data upon the subject with special reference to the biology of both the plasmodia and the mosquito vectors, malaria surveys, and prophylaxis.

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THE 1930 STATUS OF MALARIA IN THE SOUTHERN UNITED STATES, AS DETERMINED BY MORTALITY DATA*

By ERNEST CARROLL FAUST, M.D.,
New Orleans, La.

INTRODUCTION

After making a tour of the southern United States a distinguished foreign malariologist once remarked that there was no malaria problem here; we were merely annoyed by mosquitoes. While there are at the present time no such vast areas of intensive infection with malarial organisms as have in the past been recorded from French Indo-China, Siam, the Malay Peninsula, Java and Sumatra, a careful examination of the 1930 mortality rates for fourteen Southern states indicates that there is most certainly a malaria problem in our midst.

Mortality data by states as a whole, while indicative of trends in the control of the disease, are not satisfactory, since they do not designate the more circumscribed areas where heavy foci of the infection exist. For this reason, and in order that a clearer picture of the existing conditions may be obtained, the writer has secured mortality data by counties for this whole area, and has represented this situation graphically on an enlarged map. These data have been made available through the health officers of the respective states, to whom the writer desires to express his most sincere thanks.

In order to visualize the areas under control and those of mild endemicity, as well as the foci of heavy infection, the simplest type of legend has been employed, namely: white for those counties where no deaths due to malaria were recorded for the year 1930, small dots for the counties with 20 or less deaths recorded, and successively larger dots for the 20 to 50, 50 to 100 and 100 to 200 groups, while solid black indicates a mortality of more than two hundred per 100,000. The counties are numbered by states in alphabetical sequence, with the exceptions of Texas, where such sequence applies only to the counties in the eastern part of the State, including only those shown on the map, and of Missouri, where only the southern three tiers of counties are shown.

DATA PRESENTED

An examination of the map indicates that more than half of the counties in the southern United States show some mortality; that no small portion of these has a mortality rate of more than twenty per 100,000; that sixty-six counties in the area have a mortality rate of more than fifty; that twelve counties have a mortality rate of more than 100, and that two counties have a rate of more than 200, of which one of the latter stands at 300. Surely these figures are not insignificant.

It will be advisable now to present the data by states, working from west to east.

Oklahoma.—Of the 126 counties in this State, 37 (29.3 per cent) had recorded deaths from malaria in 1930. Eight of these had a rate of more than twenty. The majority of the malarious counties border the Arkansas River and its tributaries. The rate for the entire State was 5.27. The rate has not changed perceptibly within the past five years, although there has been a net decrease within the decade of 5 counties (5.4 per cent) showing a mortality of 10 or more per 100,000.

Texas.—Only the eastern half of this State is shown on the map. Of the 159 counties represented, 77 (48.4 per cent) had recorded deaths from malaria in 1930. Eighteen of these had a rate of more than 20 for the 1929-1930 interval. The majority of the more heavily infected counties are in the northeastern part of the State, with drainage into the Red River and Sabine River. Only four counties in the western half of the State had malaria deaths during 1930 and only four for the preceding year. The rate for the State as a whole in 1930 was 5.52, which is essentially the same figure as ten years ago, although a low of 3.8 was reached in 1923 and again in 1927. Within the past ten years there has been a net decrease of 6.1 per cent of the counties showing a malaria death rate of 10 or more per 100,000.

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*From the Parasitology Laboratory, Department of Tropical Medicine, School of Medicine, Tulane University.

Arkansas.—Of the 75 counties in the State all but seven (9.3 per cent) had recorded malaria deaths in 1930. Of these, 45 (60 per cent of the entire State), had a rate over 20, twenty (26.6 per cent) had a rate over fifty, and one (Phillips County) had a rate of 125. The rate for the entire State for 1930 was 36.3, the same figure as for 1929 (36.2), and essentially the same as for the past ten years. This is the highest rate for any state at the present time. Within the past decade 35 counties have shown an increase above 20 per 100,000 and 28 counties a decrease, with a net increase of significant deaths in 7 counties (9.3 per cent). The heavy spots occur along the St. Francis, White, Arkansas, Ouachita and Red Rivers, particularly where the first four converge to enter the Mississippi River.

Louisiana.—Of the 64 parishes in the State, 48 (75 per cent) had recorded malaria deaths for 1930. Only eight (12.5 per cent), however, had a rate above 20 and none as high as 50. (33.5 for Madison Parish was the highest record for the year.) With few exceptions malaria has decreased year by year in Louisiana and in 1930 the average rate for the State was 8.5, or only one-fourth of that for 1920. The more severe foci of infection are found along the Red and Tensas Rivers, while the rice-growing parishes and those along the southeast coast are now essentially malaria-free. Altogether within the past ten years there has been a net decrease of the significant death rate in 47 parishes, or 73.4 per cent of the parishes in the State.

Missouri.—Of the 33 counties in the southern three tiers in this State, 14 (42.4 per cent) reported deaths due to malaria in 1930. Of these ten (30.3 per cent) were in excess of 10 per 100,000, and three (Butler, Dunklin and Pemiscot) were somewhat in excess of 50. In addition, 13 counties farther north in the State reported one to six deaths from malaria during the year. As compared with 1919-1921 (Maxcy, 1. c.) 5 counties showed an increase in the rate above 10 per 100,000 and 7 showed a decrease, making a net gain of 6.1 per cent.

Kentucky.—Only 25 of the 120 counties in this State had recorded deaths caused by malaria in 1930. Of these only three had a mortality rate over 20. These latter are situated in the extreme western part of the State, adjacent to the Ohio and Mississippi Rivers. The rate for the State as a whole for 1930 was 2.1. An increase of 3 counties with a significant death rate has occurred within the decade.

Tennessee.—Of the 95 counties in the State, 32 (33.6 per cent), had recorded deaths due to malaria in 1930. All of the counties with a rate over 20 (10 or 10.5 per cent) are situated between the Mississippi and the Tennessee Rivers. The average rate for the State was 5.4 in 1930, which shows a continued decrease in the rate since 1921, when the average was 15.2. The net number of counties with a rate of 10 or more has decreased by 9 or 9.5 per cent within this period.

Mississippi.—Of the 82 counties in the State, all but 13 (15.8 per cent) recorded deaths from malaria in 1930. Eighteen (21.9 per cent) of the positive counties returned a rate of more than 20, although only one (Tunica County) had a rate exceeding 50 (61.2). Except for the Mississippi-Yazoo Delta region, where a block of ten counties has a rate in excess of 20, the remaining counties of heavy endemicity are scattered, northeast, southeast, and coastal. The average rate for the State in 1930 was 13.9, the lowest figure reached in Mississippi's fight against the infection. During the past decade the net decrease in the number of counties with a rate of 10 or more amounts to 63, or 76.9 per cent.

Alabama.—Of the 67 counties in this State, only 9 (13.3 per cent) were without deaths from malaria in 1930. Sixteen counties (23.8 per cent) had a rate exceeding 20 and two (Greene and Houston Counties) had a rate slightly more than 50. The regions of heavy infection lie between the Tombigbee and Alabama Rivers and in the lower valley of the Chattahoochee. The average malaria mortality rate for the State for 1930 was 11.27, a decrease from 1929 and approximately the same as for the year 1928, but in excess of the 1923-1927 rates. Within the past ten years there has been a net increase amounting to fourteen, or 20.9 per cent, in the number of counties, with a malaria death rate of ten or over.

Georgia.—Of the 161 counties in this State, 96 (59.6 per cent) had deaths recorded as due to malaria in 1930. Forty-seven of these (29.2 per cent) had a rate exceeding 20; thirteen (8.1 per cent) in excess of 50; four in excess of 100, and one (Jenkins County) had the exceedingly high rate of 208. Practically all of the severely endemic region stretches through the limestone belt from the southwestern corner northeastwardly toward the South Carolina line. The extreme north and the extreme south are essentially without heavy foci. The average rate for the State for 1930 was 15.2, a lower level than for 1928 or 1929, but considerably in excess of the years 1925-1927. Since 1921, 54 counties have shown an increase and 40 counties a decrease in the malaria mortality rate exceeding 10 per 100,000, making a net increase of 14 counties.

Florida.—Of the 67 counties in this State, 50 (74.6 per cent) recorded deaths due to malaria for the year 1930. Thirty-four of these (50.7 per cent of the whole group) had a rate exceeding 20; fourteen (28.4 per cent of the total) had a rate between 50 and 100; four (Citrus, Jefferson, Levy and Wakulla Counties) ranged between 100 and 200, and one (Dixie County) reached the 1930 peak for the United States with a rate of 300 per 100,000. This last, although computed for a relatively small area, exceeds the 1927-1929 rate by 50 per cent and compares with the rates for the swamp areas of southeastern Missouri some twenty years ago. These areas of heavy endemicity are all in the lower drainage of rivers flowing into the Gulf, but particularly in the lower Sewanee Valley. The average rate for the State for 1930 was 21.67, which indicates a 50 per cent decrease from 1928 and 1929, but a slight

increase over the 1925-1927 period. On the whole there has been no marked change in Florida during the past decade. Within the decade the net number of counties showing a malaria death rate of 10 or over has increased by 5, or 7.5 per cent.

South Carolina.—Of the 46 counties in this State, 33 (71.7 per cent) had malaria deaths recorded for 1930. Eighteen of these (39.1 per cent of the total) had a rate exceeding 20, eight (17.4 per cent of the entire group) had a rate above 50, and 2 counties (Beaufort and Berkeley) had a rate in excess of 100 (174.42 and 144.0, respectively). All of these counties, which are heavily malarious, lie in the lower coastal drainage plain of the Atlantic. Comparable to Beaufort in situation, however, is Charleston County, with a malaria mortality rate of only 16.66, or approximately one-tenth of the former county. The average rate for the State is 19.26, a figure slightly lower than those for 1928-1929, but nearly twice that for the minimum year of 1925 (rate 10.7). Since 1921 there has been a net increase of 5 (10.8 per cent) in the number of counties with a malaria death rate of 10 or more.

North Carolina.—Of the 100 counties in this State, only 26 reported deaths from malaria in 1930, and only one (Washington County) had a rate in excess of 20 (25.8, based on three deaths). The rate for the State as a whole for 1930 was 1.4, the lowest in the State's malaria records, and less than one-fifth of that of the years preceding 1921. Altogether there has been a net decrease of 23 (23 per cent) in the number of counties showing a rate of 10 or more.

Virginia.—Of the 100 counties in this State, 13 reported deaths from malaria for the year 1930. Only one (Middlesex County) had a rate in excess of 20 (27.4, based on two deaths). The rate for the entire State for 1930 was 0.62, slightly higher than the lowest record of 1928, but otherwise a minimum record and only one-third of the rate for 1921. A net decrease of 3 counties having a death rate of 10 or more is recorded for this State during the past decade.

DISCUSSION

In the area covered by this map there are altogether 1,243 counties, of which 646, or 51.9 per cent, reported deaths from malaria in 1930. Of these malarious counties 412, or 33.2 per cent, had a mortality rate less than 20 per 100,000; 168, or 13.5 per cent, had a rate between 20 and 50; 54, or 4.3 per cent, had a rate between 50 and 100; and 12, or 0.9 per cent, had a rate in excess of 100 per 100,000 popu'ation.

In some counties and states the 1930 malaria mortality rate represents a slight increase over the 1928 or 1929 figures; in other counties and states it shows a satisfactory decrease. On the whole, the picture presented for 1930 is fairly indicative of the present status with respect to malaria in our Southern states. A comparison with the figures of Maxcy (1923) for 1919-1921 for this area indicates the following trends:

(1) A decrease in the rate has been made on the Oklahoma side of the Red River valley, although the infection appears to be considerably more widespread in Oklahoma than it was a decade ago. The same conclusions apply to coastal Texas.

(2) With respect to intensity southeastern Missouri and Arkansas show a satisfactory reduction, although more counties in Arkansas reported deaths from malaria in 1930 than are indicated in Maxcy's data (1923). The Mississippi-St. Francis-White-Arkansas Delta region is still a very important hotbed of malaria.

(3) A marked decrease throughout all of the malarious districts of Louisiana is noted. The control of the disease in northern Louisiana is particularly gratifying.

(4) Malaria is somewhat more widespread in western Kentucky today than it was a decade ago.

(5) Progress in the control of malaria in western Tennessee is relatively satisfactory.

(6) Marked decrease in intensity of the disease is noted for the Yazoo-Mississippi Delta region.

(7) The situation in Alabama, Georgia and Florida is essentially unchanged. Effective control in these states still requires actual demonstration.

(8) In the coastal region of South Carolina malaria is still a major public health problem.

(9) In North Carolina gratifying diminution in the intensity of malaria deaths is noted, although there is apparently a slight increase in the extent of the mortality records.

(10) Except for Midd'esex County on the lower Rappahannock River, the situation in Virginia appears to be much improved.

(11) The following states show a notable decrease in the number of counties reporting a malaria death rate of 10 or more per 100,000: Texas, 36 (22.7 per cent); Louisiana, 47 (73.4 per cent); Mississippi, 63 (76.9 per cent); and North Carolina, 23 (23 per cent). The following states show a slight decrease: Missouri, 2 (6.1 per cent); Oklahoma, 4 (5.4 per cent); Tennessee, 9 (9.5 per cent); and Virginia, 3 (3 per cent). The following states show a net increase: Alabama, 14 (20.9 per cent); Arkansas, 7 (9.3 per cent); Florida, 5 (7.5 per cent); Georgia, 14 (9.6 per cent); Kentucky, 3 (2.4 per cent); and South Carolina, 5 (10.8 per cent).

(12) A total of 214 counties (17.2 per cent) in the southern United States show a death rate from malaria of 10 or more for 1930 in excess of the 1919-1921 rates of these counties. On the other hand, 363 counties (29.1 per cent) which had a rate of 10 or more during 1919-1921 have a rate for 1930 of less than 10. This makes a net significant reduction of 149 counties (11.9 per cent) and may be considered as a rough estimate of the reduction which has taken place during the past decade.

Maxcy (in a private communication) has indicated to the writer that it is not safe "to draw any conclusions as to whether the disease has increased or decreased in a county on the basis of a single year's experience." This is a logical deduction and merits

MALARIA MORTALITY
IN THE SOUTHERN STATES
FOR THE YEAR 1930
Rate per 100,000 population
LEGEND
DEATHS per 100,000 POPULATION.
NO DEATHS REPORTED.
0.1 TO 20.0 DEATHS per 100,000
20.1 TO 50.0 DEATHS per 100,000
50.1 TO 100.0 DEATHS per 100,000
100.1 TO 200.0 DEATHS per 100,000
200.1 OR MORE DEATHS per 100,000
Compiled and drawn by
Dr. Ernest Carroll Faust
Department of Tropical Medicine
Tulane Medical School
New Orleans, LOUISIANA.
MISSOURI
OKLAHOMA
ARKANSAS
TENNESSEE
MISSISSIPPI
KENTUCKY
VIRGINIA
NORTH CAROLINA
SOUTH CAROLINA
GEORGIA
FLORIDA
TEXAS
LOUISIANA

careful consideration. Two heavily malarious states, Arkansas and Florida, for which data are available for the past five years, have therefore been examined and the mortality rate averages for the five-year period 1926-1930 computed. In Arkansas 15 counties (20 per cent) have an average which varies somewhat from the 1930 rate. Five of these counties have an average increase and ten have an average decrease varying from the 1930 figures. In other words, the average rate is about 6.6 per cent more favorable than the 1930 rate. In Florida the average rate for the five-year period deviated somewhat in six counties (8.9 per cent) from the 1930 rate. Two of these had an average increase and four had an average decrease varying from the 1930 figures, with a net favorable decrease of two (slightly less than 3 per cent). If comparable variations exist in the other states there will be evidence that more deaths from malaria per 100,000 population were recorded in 1930 than in the average year for the five-year period. However, this difference is not enough to affect significantly that comparison with figures which Maxcy compiled for the 1919-1921 period.

Undoubtedly the more accurate diagnosis of the infection at the present time may also have influenced the number of recorded deaths in the area. It is impossible to estimate whether more complete registration during more recent years and more accurate diagnoses would have influenced the mortality rate favorably or unfavorably.

Unfortunately mortality data, although the most accurate measure of malaria at the present time for any large registration area, only provide an approximate estimate of malaria morbidity. This is due to several causes, of which the most important is perhaps the fact that most of the deaths from malaria in the southern United States are probably due to infection with *Plasmodium falciparum*, whereas *Plasmodium vivax* unquestionably has a wider distribution. It is therefore necessary to recognize the limitations of any mortality statistics such as the writer has been obliged to utilize. It is a matter of keen regret that there are not available for the entire area reliable morbidity data such as exist for limited areas where intensive studies have been carried on.

GENERAL CONCLUSIONS

While satisfactory decreases have occurred in the mortality rate for malaria in certain regions of the Southern states, there are extensive areas where the rate is essentially the same as it was a decade ago. Although a decrease in the number of deaths has been effected in certain counties of certain states, an increase in the counties reporting deaths due to the disease is reported. In other states rates in excess of 10 per 100,000 population have apparently become more common than they were a decade ago. There is abundant evidence to indicate that malaria is still a major public health problem in the southern United States.

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DISCUSSION (*Abstract*)

Dr. F. L. Hoffman, Newark, N. J.—Dr. Faust has pointed out to us that there are states, like Arkansas, in which as many as 91 per cent of the counties are affected by malaria, while the proportion runs as low as 13 per cent in Virginia. The present picture, however, is in marked contrast to the past, for in former years the entire Atlantic coastal plains of the Southern states were heavily infected, while now large areas are comparatively free from the disease. But the malaria problem in the South is still one of vast extent and of considerable complexities. There are still areas where the mortality may reach as high as 200 per 100,000, corresponding somewhat to the heavily infected areas on the west coast of Africa. I agree with Dr. Faust that the present-day trends of malaria are not suggestive of successful control and that much requires to be done. But the disease must be studied with particular reference to specific localities and sections rather than by states as a whole.

For some of the states the conclusions of Dr. Faust are rather disconcerting. In Oklahoma, for example, the disease has spread considerably during recent years, and the same is true of the coastal plains of Texas. In the lowlands of Mississippi and Arkansas the disease is still exceedingly common. In Louisiana, however, there has been a marked decrease in all the malarious districts. In western Kentucky the disease is now more common than it was ten years ago, but the control of the disease in western Tennessee is apparently successful. A very marked decrease in intensity is noted for the Mississippi-Yazoo Delta region. The situation in Alabama, Georgia and Florida remains apparently unchanged. In the coastal region of South Carolina malaria is still a major health problem, but happily considerable progress has been made in North Carolina, where formerly the disease was extremely common in the coastal plains. With the exception of a few counties, the situation in Virginia is apparently under control.

The conclusions of Dr. Faust support my own investigations extending over many years. I, also, in season and out, have emphasized the urgency of thoroughgoing malaria surveys to localize the intensity of the disease and the sources of infection. The excessive incidence of malaria requires to be taken much more seriously than has generally been the case, since malaria complicates deaths from many other causes, especially diseases of the renal organs.

Dr. K. F. Maxcy, University, Va.—I have been very much interested in Dr. Faust's analysis of the 1930 malaria mortality figures in comparison with those of 1919-1921. Mortality reports furnish the only data available, unsatisfactory though they be, for a general survey of the malaria situation in the southern United States. While accurate surveys by means of blood and spleen indices have been conducted in many localities, they afford no basis for generalization.

There is no doubt that mortality rates based upon the county as a unit of population can be used in a rough way to mark out the geographic distribution of the disease and to indicate the areas of relatively high, low or questionable prevalence. Intensive field studies of limited localities have, in a general way, supported the inferences made in the 1919-1921 analysis of county malaria rates.

On the other hand, as experience has accumulated, it has become increasingly evident that the errors of malaria death registration, due to degree of completeness, due to inaccuracies of diagnosis, and due to the chance variation of small numbers when the county is used as a unit of population, are so imponderable as sharply to restrict the use of the data.

For example, where Dr. Faust has noted an increase or a decrease in the malaria mortality rate of a county in 1930 as compared with 1919-1921, the difference is due to an indeterminate degree to the errors mentioned. It does not necessarily imply a corresponding increase or decrease in intensity or prevalence of the disease. His observations with regard to the more widespread distribution of infection in Oklahoma, coastal Texas and western Kentucky may be due largely, if not entirely, to the improved registration of deaths which is known to have taken place during this period. Such changes as have been mentioned in registration of deaths are particularly apt to occur in counties in which there has recently been established a full-time health organization.

In view of past experience, American workers can well afford to be cautious and conservative in the use of malaria statistics. County mortality figures can be used to block out the extent of the problem in a rough way, but small differences do not warrant statements as to the increase or decrease of the disease without knowledge of the local situation.

Finally, I hope that Dr. Faust will not think me too argumentative if I beg to disagree with his final statement: that malaria is still a major public health problem in the southern United States. I would qualify that statement to the effect that malaria is still a public health problem of major importance in certain limited localities of the southern United States which are now well known. The great majority of people and most of the land area of this section are as safe from malaria as are the people and land in the northern United States.

Dr. H. E. Meleney, Nashville, Tenn.—Although it is well recognized that mortality statistics have a limited value in estimating the amount of malaria in a region, they have somewhat greater value in comparing the amount of malaria present in different regions having the same general environmental conditions. In Tennessee it was found that the mortality rate from malaria in the counties bordering on the Mississippi River correspond, with but one exception, with the morbidity rate as indicated by county-wide blood surveys of the school children. Dr. Faust has used only one year in presenting his figures on malaria mortality in the southern United States and the year which he chose, 1930, being a drought year is perhaps not representative of the trend of malaria in this country. In Tennessee, where county-wide surveys were made during 1930, the incidence was found to be very much lower than in 1929, due undoubtedly to the drought. An increase in malaria is to be expected in the future in the presence of normal conditions of rainfall.

Dr. Faust (closing).—I wish to agree with those discussing my paper that mortality data certainly are a frail skeleton from which to draw conclusions. However, they are the best we have and it will be interesting ten years from now to compare the mortality maps with those of 1930.

SOME RECENT INVESTIGATIONS OF THE VIABILITY AND LONGEVITY OF THE MALARIA PARASITE IN THE MOSQUITO AS RELATED TO MALARIA THERAPY OF PARESIS*

By BRUCE MAYNE, D.P.H., M.Sc.,†
Columbia, S. C.

In inducing malaria for therapeutic purposes the general method in vogue of transferring blood directly from one general paralytic to another is not infallible. The injection of blood is questionable when the diagnosis is not clearly defined. Some authorities object to using blood which comes from a paretic, on account of the possibility of conveying foreign substances, neurotropic and other strains of syphilis. However remote the possibility, one may encounter a bacterial infection, similar to that observed at one of the state hospitals. In this instance, following the inoculation of blood in malaria therapy, it was realized that the blood donor was suffering from a streptococcus infection which subsequently proved fatal. One of the three cases receiving the blood likewise succumbed to a similar bacteremia. The possibility, less remote, of having a mixed infection of malaria parasites was demonstrated from personal observation in three distinct centers of malaria therapy. In two hospitals fatal instances were noted as the probable result of confusing mixed parasites of malignant tertian and simple tertian. In another institution blood used to convey simple tertian malaria was observed to harbor both quartan and tertian forms, predominantly the former. All of this gives emphasis to the need for conducting more of our malaria therapy through the agency of anopheline mosquitoes: a method up to the present, however, far from the ideal and probably subject to more or less serious objections.

Recognizing the risk of infecting with two kinds of parasites at the same time, the English authorities in 1925 inaugurated the inoculation of the paretic through the agency of mosquitoes. Since that time figures

*Read before National Malaria Committee (Conference on Malaria), meeting conjointly with Southern Medical Association, Twenty-Fifth Annual Meeting, New Orleans, Louisiana, November 18-20, 1931.

†Special Expert, U. S. Public Health Service.

based upon results of treatment show that among more than three thousand patients over 20 per cent were improved enough to be sent home, and approximately 12 per cent were considered permanently cured.

Of the modifications introduced into the treatment by the English workers, the most important consisted in not stopping the fever after seven or eight attacks, but allowing it to continue, modified if necessary by the judicious use of quinine, until the patient acquired tolerance for the parasite and the symptoms were not very marked. This modification is based on the hypothesis that the curative action of the malaria is not due to the fever alone, but also, and chiefly, to the continued presence of the parasites and their toxins in the patient's body.

Another modification is the use of the pure quartan strain of parasite instead of the tertian, because this parasite causes high temperature without serious symptoms, and may, therefore, be allowed to run for several weeks or even several months. Furthermore, the use of the parasite of malignant tertian, that is, estivo-autumnal, malaria, has been tried in about sixty cases in the hope that it will prove to be more active because of its tendency to sporulate in the central nervous system and other organs instead of the peripheral blood.

These modifications, particularly the allowing of the infection to continue up to the point of an acquired tolerance for the disease, are not only considered improvements in the application of malaria therapy for general paralysis, but they also furnish exceptional opportunity for the clinical and experimental therapeutic study of malaria.

In the course of undertaking malaria therapy by mosquito inoculations of patients with paresis conducted by the United States Public Health Service, the methods employed at the present time are limited to personal transportation of infected Anopheles from one institution to another in iced containers and the limited application in the sending of mosquitoes by express to trustworthy workers in Government and state institutions. All of this centers about the potentiality of the mosquito as a carrier and a conserver of the infection for more or less limited periods. The interesting queries which arise are how long mosquitoes will carry infection, and how many bites are required to infect a person. It is generally understood that mosquitoes may remain infected as long as they live. This has never been proved, however, but it has been suggested in the work of British authorities in England and in our own work here.

British investigators have actually carried mosquitoes with the malaria parasite in their hospitals for a period of ninety days and have kept mosquitoes alive fully six months for this purpose. They have found, however, that the mosquito gradually loses its infectivity after about ninety days. We have carried investigations to the point where we can confirm the work of the British authorities. It may be interesting to note that mosquitoes, following the technic in vogue at present, have been kept alive for the following periods: Anopheles, 231 days; culex, 265 days. Forms indistinguishable from sporozoites have been found in the mosquito after 155 days, however in a condition not thought to be viable on inoculation. We have maintained the parasite alive in the mosquito for a period of 55 days. Experience in India gives us the information that parasites of bird malaria, which in the insect host are difficult to distinguish from the human strain, have been carried over in the common culex mosquito, *Culex quinquefasciatus*„ for a period as long as the insect remained alive, namely, a duration of 183 days.

A word as to the transportation of live mosquitoes. This can be managed through ordinary post or by express or as hand baggage or checked baggage by ordinary train travel. We have found no difficutly in keeping mosquitoes in prime condition by these various methods, if moisture and low temperature are provided. Even in India, I have shipped mosquitoes long distances by merely surrounding the netted cage by moistened gauze pads. In fact, one of my co-workers in India has been successful in transporting live mosquitoes from India to London by this means. You may remember that the first mosquitoes were transported from Italy to London in this manner in the historical experiment of Sir Patrick Manson some thirty years ago.

During cold weather one can actually send a few mosquitoes in a mailing tube for short distances, but I would not recommend this method publicly, as there are objections at present to shipping mosquitoes, especially by aeroplane, over countries not yet free of yellow-fever.

Relation of Temperature.—Many observations tend to confirm the general impression that the gametocyte is less virile than the sporozoite. The gamete apparently requires a higher temperature for existence and development, which reflects on its origin from the warm-blooded host, and is possibly a matter of adaptation. The sporozoite has a greater range of adaptability, surviving temperatures of freezing to as high as 122° F., an adaptation to an environment afforded by the cold-blooded mosquito host.

If a batch of anophelines is placed, after biting a suitable person, in an atmosphere under 60° F., the gametocytes taken with the host's blood either fail to exhibit exflagellation or gametogenesis is otherwise rendered innocuous, the sporogonic cycle receiving a decided check. On the other hand, a batch of mosquitoes may be exposed to temperatures as low as 32 to 38° F. if the cyclical development has been encouraged to the sporozoite stage. Therefore, one must seek an optimum for the existence of the mosquito host and the perpetuation of its parasite.

High temperatures, 80° F. and above, having been repeatedly shown to be unfavorable to length of life of the artificially maintained insect, our procedure is to keep the infecting mosquito (when not applied to the patient) at temperatures averaging 76° F. during the period when sporozoites are developing, and

following this, at temperatures of a well kept cold room of the hospital morgue at 38 to 40° F. They are subsequently shipped when required at temperatures of a portable refrigerator, maintained at 38° F. or below.

The potentiality of the mosquito is emphasized when one realizes that a single mosquito may infect a great many persons. It was shown by the British authorities that a single batch of mosquitoes could be used to infect as many as forty persons, and we have shown in some former work that a single mosquito may actually infect eleven persons.

The matter of viability and resistance of the sporozoites in the mosquito is engaging our attention at present on account of the possibility of using sporozoites in suspension in various media, and thus obviating the difficulty of carrying live mosquitoes from place to place. This work has been inaugurated in the South Carolina State Hospital, and for the first time we have been successful in producing malaria by inoculating a patient with sporozoites in citrate suspension.

Up to the present time we have tried out preservation of sporozoites with a variety of sugars, glycerin, citrate, and ordinary physiological salt solutions, and find that the sporozoite, however resistant in the mosquito, is easily destroyed *in vitro* when in contact with these reagents. It may be pointed out that sporozoites persist in a mosquito long after its death, and we have recovered sporozoites from dead mosquitoes fully 48 hours, more recently 65 hours, after the insect has died. Also, we have shown that although the mosquito may be killed by heat at a temperature of about 43 to 45° C., the sporozoites, on dissection, show viability. We have observed that to kill the sporozoites it is necessary to apply heat very close to 50° C. (122° F.).

Two experiments of recent development have not been sufficiently matured for final report, but are mentioned in the hope that interest in this direction may be stimulated. Twelve patients have been inoculated with sporozoites washed from the infected mosquitoes' stomach, as well as from the salivary glands.

It has been found possible to keep the mosquitoes' oocyst infected gut and wash it at intervals during the course of 72 hours while the newly ripened oocysts are discharging the accumulated sporozoites into the sterile mounting medium.

It is possible to collect this material after four successive crops of sporozoite discharges.

DISCUSSION (*Abstract*)

Dr. M. A. Barber, New York, N. Y.—I have had some experience with the transporting of living malarial mosquitoes. Last May we sent some from West Africa to London. We put them on a steamer in the hands of the ship's surgeon. When the ship arrived at Plymouth they were put in charge of the quarantine officer and he put them in care of the train guard. When they arrived in London they were met by a representative of the Board of Health.

Dr. Mayne (closing).—In malaria therapy the mosquito inoculation method could be enhanced in value by applying the mosquito to the patient in biting by the interrupted method. As you are aware, it has been proved that a bite of twenty to thirty seconds is productive of infection and is equal in effectiveness to that of an uninterrupted blood meal of eight to ten minutes.

One may thus conserve the sporozoite contents of the salivary lobes and by the mechanism of limited discharge distribute the full crop by applying the mosquito to an unlimited number of patients.

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LIGHT AND THE CAUSATIVE AGENT OF A MALIGNANT FOWL TUMOR

The eye sees and differentiates as shades of red, yellow, green, blue, light of a certain wave length, fails to see light of shorter wave lengths, such as the ultraviolet which heals rickets, and another ultraviolet which produces tanning of the skin. A still shorter invisible ray, the x-ray, penetrates the skin, "lights" the interior of the body, and is one of the most effective clinical agents for destruction of cancer cells. A slightly longer ray than the x-ray, the grenz ray, destroys malignancies on the skin surface, but does not penetrate the deeper tissues.

Modern physics has made possible the remarkable practical utilization of invisible light in the x-ray and the radio; and has produced machinery which will give off radiation of nearly any desired periodicity. Monochromatic, or one wave, light of different accurately delivered wave lengths is available for physiological research. Most of these radiations affect living cells variously and specifically, and in this specificity lies one of the important leads to differentiation of cellular reactions and destruction of malignant tissue.

Sturm, Gates and Murphy,[1] of the Rockefeller Institute, have studied the effects of several different wave lengths of ultraviolet light upon malignant chicken tumors and their causative agents. They have calculated the quantity of light at each wave length necessary to inactivate the tumor filtrates. Sarcoma cells of fowls, they say, are rather susceptible to ultraviolet radiation. On the contrary, the etiological agent of fowl sarcoma, which may be filtered from the cells, is resistant. It continues to infect birds after a considerable exposure to ultraviolet radiation. Bacteria such as the streptococci are easily destroyed by ultraviolet light, while eight times the lethal dose for bacteria does not affect the virulence of the tumor agent.

As a contribution to the study of the filterable fowl tumors, the Rockefeller workers have prepared curves, showing the amount of radiation at each of a number of wave lengths in the ultraviolet region which was necessary to destroy the tumor filtrate. For comparison, they determined the quantity of the same light required to destroy several types of bacteria, a vaccine virus, and a bacteriophage. The tumor agent was the most difficult to destroy of all these. It required greater exposure, it "died" last, at every wave length. It required less radiation, however, than that needed for destruction of some of the enzymes.

In its reaction to light of this type, therefore, the tumor agent resembled an enzyme rather than the bacteria of an infectious disease.

HUNGER, VITAMIN B, AND THE THYROID

Failure of children's appetites is one of the common complaints of mothers of the present day, who solicitously stand over their offspring at mealtimes directing and persuading them to eat. In older days, dining was a privilege accorded to good children, not a sacred duty to parents. To be sent from the table or put to bed without supper was a disagreeable but not an infrequent punishment. It is of course a human weakness to yearn away from anything

1. Sturm, E.; Gates, F. L.; and Murphy, J. B.: Properties of the Causative Agent of a Chicken Tumor: Inactivation of Tumor Producing Agent by Monochromatic Ultraviolet Light. Jour. Exper. Med., 55:441, March, 1931.

that one ought to do. If mealtime could again take the place in the mind of a pleasant reward of virtue instead of a call of the "Stern Daughter of the Voice of God," Duty, the child might be conditioned to enjoy this essential activity. Similarly with adults.

This is merely one of the possible psychic causes of anorexia. There are a number of physical bases as well. Failure of a dog's appetite would rarely be due to psychic factors. A progressive anorexia may be produced by deficiency of vitamin B, in which condition animals gradually lose all interest in food placed before them. Certain quantitative relationships have been shown between this vitamin and the number of calories which can be metabolized. As the biochemists express it, the quantity of vitamin B divided by the number of calories is a constant, which they call K. As the calory intake is increased the vitamin B content of the diet must be greater, because K does not change. Given a certain number of calories without vitamin B, the appetites of animals fail at a predictable time, and they will starve to death in the presence of much food. Hunger and weight maintenance thus depend upon the supply of vitamin B, as well as upon the available heat units of the dietary.

Hyperthyroidism is often accompanied by an increased appetite. It was thought possible, therefore, that the thyroid hormone might substitute for vitamin B and stimulate animals on a B deficient diet to eat. Himwich, Goldfarb and Cowgill,[1] of Yale University, administered desiccated thyroid gland to dogs till the basal metabolic rate increased, and gave them at the same time a diet in which vitamin B was lacking. Instead of increasing the food consumption, the addition of thyroid hastened the onset of anorexia. Failure of appetite appeared in one-third the time required in control animals which were receiving a B deficient diet without thyroid. The loss of weight and depletion of the liver glycogen reserves which characterize hyperthyroidism could be prevented by a liberal allowance of vitamin B, and the hyperthyroid animals could be kept in normal condition merely by increasing their calories and proportionately their supply of vitamin B.

Experimental anorexia appears to be more specifically related to deficiency of this food element, vitamin B, than to any other known factor. In hyperthyroidism, the organism is peculiarly sensitive to a shortage of it, because the energy requirement is increased, and when anorexia accompanies a high basal metabolic rate the goiter syndrome is apt to be rapidly exaggerated. Attention to vitamin B intake in this condition is essential, since with proper dietary care a mild hyperthyroid might live comfortably and remain free from symptoms of his disease for a considerable period.

1. Himwich, H. E.; Goldfarb, W.; and Cowgill, G. R.: Studies in Physiology of the Vitamins: Effect of Thyroid Administration Upon the Anorexia Characteristic of Undifferentiated Vitamin B Deficiency. Amer. Jour. Physiol., 99:689, Feb., 1932.

GLEANINGS FROM RECENT JOURNALS

Modification of the Aschheim-Zondek Pregnancy Test.—In the Aschheim-Zondek pregnancy test and its commoner modifications, urine of the patient is injected into a small laboratory animal, the ovaries of which are subsequently examined for Graafian follicles. Brown,[1] of Washington University, St. Louis, has reported on a series of tests in which blood serum of the suspected woman was used instead of urine. Two to five c. c. of serum of 230 women were injected intravenously into rabbits. He reports that the diagnoses were approximately 100 per cent correct. The reactions were more marked than with urine and they occurred more promptly.

Blood of many non-pregnant women at various times in relation to the menstrual cycle should be examined before this modification is widely accepted. Establishment of normals for the hormone content of blood and urine of women at different times in relation to ovulation will aid in gynecological diagnosis. It has been noted that in pregnant women who abort, the urinary anterior pituitary hormone diminishes. This is an important field for investigation. Specimens of urine are always more easily available for analysis than blood which must be obtained by venipuncture. Urine is therefore more desirable for routine clinical tests.

Diagnosis of Congenital Syphilis in the Newborn.—Infants of syphilitic mothers are usually

1. Brown, T. K.: A Proposed Modification of the Aschheim-Zondek Pregnancy Test. Amer. Jour. Obst. & Gyn., 23:379, March, 1932.

regarded as syphilitic and treated as such if their Wassermann is positive. A transitory positive Wassermann may be found, however, in the infants of syphilitic mothers in the first two weeks after birth, which does not mean infection with the spirochete, and which disappears without treatment.[1] It is probably caused by antibodies which pass from the maternal to the fetal blood through the placenta. A positive tuberculin test similarly may be obtained from the healthy child of a tuberculous mother.

If the Wassermann reaction in the first few weeks of life weakens without treatment, according to Dunham,[2] of Yale, and symptoms are absent, the child is not syphilitic. He reports 14 infants of syphilitic mothers, the infants having positive Wassermann reactions within the first two days after birth, but no symptoms of syphilis. Upon re-examination after two weeks, the Wassermann was perceptibly weaker. Spinal puncture was not done. The x-rays of the long bones were normal. Although three babies had palpable spleens and two had transient snuffles, treatment was withheld from all. One premature infant of the series died at 39 days. Necropsy showed no evidence of syphilis. The other thirteen were well when last examined after a considerable period had elapsed.

It is important, he believes, not to attach the stigma of syphilis unnecessarily to an infant, and not to claim an easy cure because treatment was instituted early and the Wassermann became negative.

Fat and Sucrose in Highly Purified Diets.— It has been believed in some quarters that fat was not actually a necessary component of the diet, that if the fat-soluble vitamins could be supplied, fats themselves could be dispensed with. But sucrose cannot function as the sole source of energy, according to work of Evans and Lepkovsky,[3] of the University of California. Neither can all the energy for body needs be derived from fat. Some sucrose is necessary. Normal growth is impossible on a fat-free or sugar-free diet. Very small quantities of certain unsaturated fatty acids, for example, linoleic acid, markedly improve the condition of animals on a high sucrose, fat-free diet.

All animal deficiency diseases have some clinical possibilities and interest, though it is unlikely that human beings in this country would subsist upon a diet wholly free from fat. The symptoms of an experimental fat-free diet in the California laboratory were impairment of growth, dermatitis, with scaliness of the skin and tail; and an abnormally large intake of water was regularly noted. There were kidney lesions, and blood was observed in the urine. Necessity for a diversified natural diet for human beings is further emphasized.

2. Dunham, E. C.: Diagnosis of Congenital Syphilis in the Newborn. Amer. Jour. Dis. Child., 43:317, Feb., 1932.
3. Evans, H. M.; and Lepkovsky, Samuel: Beneficial Effects of Fat in High Sucrose Diets when Requirements for the Antineuritic Vitamin B and the Fat-Soluble Vitamins Are Fully Satisfied. Jour. Biol. Chem., 92:615, Aug., 1931. Idem.: Vital Need of the Body for Certain Unsaturated Fatty Acids. Experiments with Fat-Free Diets in which Sucrose Furnishes the Sole Source of Energy, p. 143, April, 1932. Experiments with High Fat Diet in Which Saturated Fatty Acids Furnish the Sole Source of Energy, p. 157, April, 1932. Sparing Action of Fat on Vitamin B, p. 165, April, 1932.

Book Reviews

Manual of Surgery. Volumes II and III. By Alexander Miles, M.D., LL.D., F.R.C.S.Ed., Consulting Surgeon, Royal Infirmary, Edinburgh, and D. P. D. Wilkie, M.D., F.R.C.S.Ed. and Eng., Professor of Surgery, University of Edinburgh. Second volume: Extremities, head, neck. 685 pages with 303 illustrations. Third volume: Thorax, Abdomen. 578 pages with 177 illustrations. New York: The Oxford University Press, 1931. Cloth, $3.80 each.

The first volume of this set was reviewed in the SOUTHERN MEDICAL JOURNAL for August, 1931.

Volume II is concerned with surgical diagnosis of conditions in the extremities, head and neck. Volume III covers the abdomen. No detailed operative procedures are given in these manuals. The illustrations are numerous and enlightening. The undergraduate or medical practitioners will find these volumes satisfactory diagnostic aids.

Mental Nursing (Simplified). By O. P. Napier Pearn, M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, Cane Hill Mental Hospital. 304 pages with tables and charts. New York: William Wood & Co., 1932. Cloth, $2.00.

There is a brief review of important methods of study, explanation of terms, and many suggestions for the care of patients in general, as well as nervous and mental patients. Very simple yet striking pictures are used to emphasize certain facts.

Anatomy, and physiology, the professional duties of the nurse, her attitude to the patient and her moral obligations are reviewed.

The descriptions and derivations of the more common medical terms are enlightening. To the average layman interested in general medicine and the nervous system, to doctors' assistants and secretaries, this should be a most satisfactory reference.

Why this comprehensive handbook should be limited by the title "Mental Nursing" is the only obscure point in the work.

History of Medicine in the United States. Volumes I and II. By Francis R. Packard, M.D., Editor, Annals of Medical History. 1323 pages with 206 illustrations. New York: Paul B. Hoeber, Inc., 1931. Cloth, $12.00.

Dr. Packard begins his history of American medicine with accounts of the first physicians and barber surgeons who came to this country with the colonists in the early Seventeenth Century. One of the common diseases on the ships of the day was, of course, scurvy. There are vivid accounts of the epidemics of smallpox and yellow-fever through the first settled territories; of the introduction of vaccination, which was a surgical operation with elaborate purging and preparation for inoculations; of the public speeches and sermons against the practice which was said to be immoral and to show a distrust of God's overruling care; and later of the rage for vaccination. A yellow-fever epidemic was reported to have originated from a pile of decaying coffee. A bitter dispute of Benjamin Rush and his opponents through the newspapers dealt with the value of purges and blood letting in this disease.

There are sections on early medical legis'ation, hospitals, care of the insane, dispensaries, medical departments of the Army and Navy, medical education, discovery of anesthesia. Among the profuse illustrations there is a facsimile of a periodical, *The North American Medical and Surgical Journal.* Its name indicates that it covered not only all the specialties, but the whole continent. Such facts are brought out as the use of bifocal lenses by Benjamin Franklin. The book ends with the beginnings of specialism in America.

These are two thoroughly delightful volumes, which represent an achievement from a literary standpoint as well as from the medical historical side.

The Principal Nervous Pathways. Neurological Charts and Schemas with Explanatory Notes. By Andrew Theodore Rasmussen, Ph.D., Professor of Neurology, Department of Anatomy, University of Minnesota, Medical School, Minneapolis, Minnesota. 73 pages with illustrations. New York: The Macmillan Company, 1932.

The charts of the nervous pathways in this monograph, while diagrammatic, are very practical. The first chart with its explanatory notes and legends on "Relations of the Meninges to the Brain, Spinal Cord and Cerebrospinal Fluid," will indicate to the average student or diagnostician the original and practical plan which the author has evolved for presenting his material.

Additional charts of the nervous pathways with the wealth of legends, concise schemas and the brief explanatory notes make the book a valuable reference.

Handbook of Medicine. Revised by John Henderson, M.D., F.R.F.P.S. (Glas.), Physician, Glasgow Royal Infirmary. Ninth Edition. 654 pages with tables and illustrations. New York: William Wood & Co., 1932. Cloth, $4.00.

This handbook is a popular text of medicine. Several of the sections have been rewritten, namely: vitamins, some gastric disorders, pernicious anemia, arthritis deformans and encephalitis lethargica. Among the new sections are those on coronary thrombosis, bundle branch block, lues of the stomach, hepatic efficiency, cholecystography, narcolepsy and various neuroses.

Only a general view of the subject is given. There are several omissions: for examples, the newer remedies in malaria, the Semple treatment of rabies, toxoid, which is more popular for diphtheria prophylaxis than the toxin-antitoxin mixture which is discussed. As most medical students become familiar with the sphygmomanometer early in medical school the illustration is superfluous. The author tends to minimize the danger of appendicitis by saying that "Most will get well without operation."

The Prevention and Treatment of Disease. Volume III of International Studies on the Relation Between the Private and Official Practice of Medicine. Conducted for the Milbank Memorial Fund by Sir Arthur Newsholme, K.C.B., M.D., F.R.C.P. 558 pages with tables and charts. Baltimore: The Williams & Wilkins Company, 1931.

The third book of a series reporting the investigations on the relationship of private and official medicine in Europe. This volume covers conditions in England, Scotland, Ireland and Wales and concludes the survey. The work has been financed by the Milbank Memorial Fund. This book is of peculiar interest to the worker in the public health field, as it is an authoritative inquiry into cooperative medicine as practised today.

Biochemistry in Internal Medicine. By Max Trumper, Ph.D., Clinical Chemist and Toxicologist; formerly in charge of the Laboratories of Biochemistry of the Jefferson Medical College and Hospital and of the Psycho-Biochemistry Laboratory, Graduate School of the University of Pennsylvania, and Abraham Cantarow, M.D., Instructor in Medicine, Jefferson Medical College; Assistant Attending Physician, Philadelphia General Hospital; in charge of Laboratory of Biochemistry, Jefferson Hospital. With a foreword by Elmer H. Funk, M.D., Sutherland M. Prevost Professor of Therapeutics at Jefferson Medical College. 454 pages with illustrations. Philadelphia: W. B. Saunders Company, 1932. Cloth, $5.50.

Books of this type are necessary at frequent intervals. The opening chapters deal with the metabolism of different classes and elements of foods: carbohydrates, protein, cholesterol, chloride, calcium, phosphorus assimilation are described, giving the normal and abnormal metabolic course of each. Function of the kidney, liver, pancreas and stomach are discussed and changes in the body during pregnancy and lactation, without mention, however, of the recent studies of the hormones of the blood and urine in pregnancy. There is a closing chapter enumerating the chemical diagnostic features of various disorders, and there are tables of normal chemical standards.

The book plunges into the facts of each subject with no waste of words and no speculation. It is a good reference and review of the accepted beliefs regarding biochemistry in health and disease. It is for the physician, not for the laboratory worker, and detailed descriptions of laboratory procedures are scupulously avoided.

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Section on Radiology—Dr. J. C. Dickinson, Chairman, Tampa, Florida; Dr. D. A. Rhinehart, Vice-Chairman, Little Rock, Arkansas; Dr. C. H. Heacock, Secretary, Memphis, Tennessee.

Section on Dermatology and Syphilology—Dr. Emmett R. Hall, Chairman, Memphis, Tennessee; Dr. M. T. Van Studdiford, Vice-Chairman, New Orleans, Louisiana; Dr. Dudley C. Smith, Secretary, University, Virginia.

Section on Surgery—Dr. J. M. T. Finney, Chairman, Baltimore, Maryland; Dr. A. G. Brenizer, Vice-Chairman, Charlotte, North Carolina; Dr. Daniel C. Elkin, Secretary, Atlanta, Georgia.

Section on Bone and Joint Surgery—Dr. Allen F. Voshel, Chairman, Baltimore, Maryland; Dr. J. Albert Key, Vice-Chairman, St. Louis, Missouri; Dr. J. W. White, Secretary, Greenville, South Carolina.

Section on Gynecology—Dr. Lawrence R. Wharton, Chairman, Baltimore, Maryland; Dr. Percy H. Wood, Vice-Chairman, Memphis, Tennessee; Dr. John W. Turner, Secretary, Atlanta, Georgia.

Section on Obstetrics—Dr. W. Bush Anderson, Chairman, Nashville, Tennessee; Dr. E. L. King, Vice-Chairman, New Orleans, Louisiana; Dr. Richard Paddock, Secretary, St. Louis, Missouri.

Section on Urology—Dr. Russell A. Hennessey, Chairman, Memphis, Tennessee; Dr. Neil S. Moore, Vice-Chairman, St. Louis, Missouri; Dr. Earl H. Floyd, Secretary, Atlanta, Georgia.

Section on Railway Surgery—Dr. D. Y. Roberts, Chairman, Louisville, Kentucky; Dr. E. Dunbar Newell, Vice-Chairman, Chattanooga, Tennessee; Dr. J. W. Palmer, Secretary, Ailey, Georgia.

Section on Ophthalmology and Otolaryngology—Dr. W. R. Buffington, Chairman, New Orleans, Louisiana; Dr. W. Likely Simpson, Vice-Chairman, Memphis, Tennessee; Dr. W. D. Gill, Secretary, San Antonio, Texas.

Section on Public Health—Dr. J. D. Applewhite, Chairman, Macon, Georgia; Dr. Joseph W. Mountin, Vice-Chairman, Washington, D. C.; Dr. Leon Banov, Secretary, Charleston, South Carolina.

National Malaria Committee (meeting conjointly with Southern Medical Association)—Dr. L. O. Howard, Honorary Chairman, Washington, D. C.; Dr. E. L. Bishop, Chairman, Nashville, Tennessee: Dr. Charles F. Craig, Chairman-Elect, New Orleans, Louisiana; Dr. Henry Hanson, Vice-Chairman, Jacksonville, Florida; Dr. Mark F. Boyd, Secretary, Tallahassee, Florida.

American Society of Tropical Medicine (meeting conjointly with Southern Medical Association, 1932)—Dr. Frank Smithies, President, Chicago, Illinois; Dr. E. L. Walker, First Vice-President, San Francisco, California; Dr. G. R. Callender, Second Vice-President, Washington, D. C.; Dr. Henry E. Meleney, Secretary-Treasurer, Nashville, Tennessee; Dr. Damaso de Rivas, Assistant Secretary, Philadelphia, Pennsylvania.

Section on Medical Education—Dr. Kenneth M. Lynch, Chairman, Charleston, South Carolina; Dr. John Walker Moore, Vice-Chairman, Louisville, Kentucky; Dr. Ernest W. Goodpasture, Secretary, Nashville, Tennessee.

Southern Association of Anesthetists (meeting conjointly with Southern Medical Association)—Dr. H. Boyd Stewart, President, Tulsa, Oklahoma; Dr. Mary E. Hopkins, First Vice-President, Louisville, Kentucky; Dr. Dennis P. Harris, Second Vice-President, Beaumont, Texas; Dr. W. Hamilton Long, Secretary-Treasurer, Louisville, Kentucky.

Women Physicians of Southern Medical Association—Dr. Kate Savage Zerfoss, Chairman, Nashville, Tennessee; Dr. Maud Loeber, Vice-Chairman, New Orleans, Louisiana; Dr. Lillian H. South, Secretary, Louisville, Kentucky.

Woman's Auxiliary to the Southern Medical Association—Mrs. Charles E. Oates, President, North Little Rock, Arkansas; Mrs. A. A. Herold, President-Elect, Shreveport, Louisiana; Mrs. S. E. Driskell, First Vice-President, Jacksonville, Florida; Mrs. S. M. Blackshear, Second Vice-President, New Orleans, Louisiana; Mrs. J. Bonar White, Recording Secretary, Atlanta, Georgia; Mrs. M. J. Kilbury, Corresponding Secretary, Little Rock, Arkansas; Mrs. Mabel Mason, Treasurer, Lumberton, Mississippi: Mrs. S. A. Collom, Jr., Historian, Texarkana, Texas; Mrs. J. D. Perdue, Parliamentarian, Mobile, Alabama.

JEFFERSON COUNTY MEDICAL SOCIETY

Birmingham, Alabama

HOST to the SOUTHERN MEDICAL ASSOCIATION, Twenty-Sixth Annual Meeting, November 16-18, 1932

Officers, Jefferson County Medical Society

President—Dr. John D. Sherrill
Vice-President—Dr. R. G. Lovelady
Secretary-Treasurer—Dr. W. B. Hardy
Chairman Board of Censors—Dr. Cabot Lull
Immediate Past President—Dr. James R. Garber

Chairmen of Local Committees on Arrangements

General Chairman—Dr. James R. Garber
Honorary Vice-General Chairmen—Dr. James S. McLester, Dr. J. M. Mason, Dr. W. G. Harrison, and Dr. Seale Harris
Finance—Dr. Stewart H. Welch
Entertainment—Dr. Alfred A. Walker
Membership—Dr. R. H. Hamrick
Hotels—Dr. Cecil D. Gaston
Meeting Places—Dr. Porter Stiles
Publicity—Dr. H. Earle Conwell
Alumni Reunion—Dr. Edward O'Connell
Scientific Exhibits—Dr. George S. Graham
Information—Dr. A. L. Glaze
Transportation—Dr. J. A. Meadows
Golf—Dr. A. B. Harris
Trap Shooting—Dr. A. L. Atwood
Women Physicians—Dr. Melson Barfield-Carter
Ladies' Entertainment—Woman's Auxiliary, Mrs. John M. Akin, President; Mrs. Sid W. Collier, Chairman

Southern Medical News

ALABAMA

Autauga County Medical Society has elected the following officers for 1932: Dr. R. G. Shanks, Autaugaville, President; Dr. R. M. Golson, Prattville, Vice-President; and Dr. J. E. Wilkinson, Jr., Prattville, Secretary-Treasurer.

Choctaw County Medical Society has elected the following officers for 1932: Dr. H. W. Robinson, Edna, President; Dr. T. M. Littlepage, Riderwood, Vice-President; and Dr. A. D. James, Choctaw, Secretary-Treasurer.

DeKalb County Medical Society has elected the following officers for 1932: Dr. W. T. Miller, Fort Payne, President; Dr. M. T. Floyd, Fort Payne, Vice-President; and Dr. W. E. Quin, Fort Payne, Secretary-Treasurer.

Elmore County Medical Society has elected the following officers for 1932: Dr. W. M. Gamble, President; Dr. E. P. Moon, Vice-President; and Dr. W. S. Owsley, Secretary-Treasurer; all of Wetumpka.

Limestone County Medical Society has elected the following officers for 1932: Dr. J. S. Crutcher, President; Dr. W. E. Maples, Vice-President; and Dr. W. J. Donald, Secretary-Treasurer; all of Athens.

Sumter County Medical Society has elected the following officers for 1932: Dr. R. D. Spratt, Livingston, President; Dr. W. E. Allen, Ward, Vice-President; and Dr. J. S. Hough, Livingston, Secretary-Treasurer.

Dr. James S. McLester, Birmingham, recently delivered the third annual Stuart McGuire Lecture at the Medical College of Virginia in Richmond.

Dr. Thurston D. Rivers has become associated in practice with Dr. R. S. Hill, Montgomery, having resigned his position on the staff of the Division of Tuberculosis Control of the State Department of Health.

Dr. W. J. Donald, Athens, has resumed his duties as Health Officer of Limestone County, after a six months' leave of absence.

Dr. R. D. Spratt, Livingston, has been elected County Physician, and Dr. J. S. Hough, Livingston, County Health Officer of Sumter County.

DEATHS

Dr. Porter King Tait, Birmingham, aged 62, died February 25.

Dr. James Wiley Robertson, Clayton, aged 66, died February 26 of pneumonia.

Dr. Thomas Ernest Lockhart, Selma, aged 67, died January 5 of gangrene of the right lung and septicemia.

Dr. Thomas Peters Deweese, Gamble Mines, aged 71, died February 2 of cirrhosis of the liver.

Dr. Robert Merritt Davis, Birmingham, aged 57, died February 9 of heart disease.

ARKANSAS

Chicot County Medical Society has elected the following officers for 1932: Dr. E. Baker, Dermott, President; and Dr. S. W. Douglas, Eudora, Secretary-Treasurer.

Columbia County Medical Society has elected the following officers for 1932: Dr. W. H. Horn, Taylor, President; and Dr. P. M. Smith, Magnolia, Secretary-Treasurer.

Lonoke County Medical Society has elected the following officers for 1932: Dr. F. E. Utley, Cabot, President; Dr. S. S. Beaty, England, Vice-President; and Dr. O. D. Ward, England, Secretary-Treasurer.

Miller County Medical Society has elected the following officers for 1932: Dr. R. R. Kirkpatrick, President; Dr. H. E. Longino, Vice-President, and Dr. J. F. Williams, Secretary-Treasurer; all of Texarkana.

A State Conference on Child Health and Protection was held recently in Little Rock, with Dr. D. A. Rhinehart, Little Rock, presiding.

Dr. Jerome S. Levy, Little Rock, has moved into new offices in the Donaghey Building, and has limited his practice to diagnosis and treatment of diseases of the alimentary tract.

The Fort Smith Clinical Society, sponsored by the staffs of St. Edward's Mercy Hospital, St. John's Hospital, and Sparks Memorial Hospital, held their fourth meeting in Fort Smith, Tuesday, March 22nd.

At a recent meeting of the Clinical Society of the Leo N. Levy Memorial Hospital, Hot Springs National Park, the following officers were elected for the coming year: Dr. A. G. Sullivan, Chairman; Dr. W. W. Chamberlian, Vice-Chairman; and Dr. H. H. Preston, Secretary; all of Hot Springs National Park.

DEATHS

Dr. William E. Vaughan, Richmond, aged 62, died February 27, of pneumonia.

Dr. Charles Prickett, Malvern, aged 54, died suddenly February 23.

Dr. Jay Ralph Shook, Hot Springs National Park, Colonel, M. C., U. S. Army, aged 54, died March 5 in Walter Reed General Hospital, Washington.

Dr. Charles Francis Thomas, Fordyce, aged 61, died December 19, 1931, of heart disease.

Dr. Robert P. Nelson, Monticello, aged 70, died January 16 of cerebral hemorrhage.

DISTRICT OF COLUMBIA

The Kober Lecture, delivered annually at the Georgetown University School of Medicine, was delivered in April by Dr. Ales Hrdlicka, Curator of Physical Anthropology, Smithsonian Institution, Washington.

The Medical Society of the District of Columbia had as a guest speaker at a recent meeting Dr. John Alexander, Ann Arbor, Michigan.

Dr. B. O. Lewis, Assistant Surgeon, has been assigned to duty at the Relief Station, Washington.

Dr. L. L. Williams, Jr., Washington, held conferences recently in Cincinnati relative to sanitary engineering work being conducted by the Public Health Service.

Dr. N. W. Sisson, after completing two years' service, has located in Washington where he will practice oto-laryngology.

DEATHS

Dr. Michael O. Dumas, Washington, aged 64, died February 17.

Dr. James Henry Gaines, Washington, aged 83, died March 10.

FLORIDA

Jackson County Medical Society has elected the following officers for 1932: Dr. Lewis Pierce, Marianna, President; and Dr. T. H. Hudgens, Sneads, Secretary-Treasurer.

Orange County Medical Society has elected the following officers for 1932: Dr. G. S. Osincup, President; Dr. Hewitt Johnston, Vice-President; Dr. L. M. Orr, Secretary; and Dr. C. J. Collins, Treasurer; all of Orlando.

Pinellas County Medical Society has elected the following officers for 1932: Dr. O. O. Feaster, President; Dr. L. M. Gable, First Vice-President; Dr. W. G. Post, Jr., Second Vice-President; Dr. A. L. Mills, Secretary; and Dr. G. E. Miller, Treasurer; all of St. Petersburg.

Polk County Medical Society has elected the following officers for 1932: Dr. J. L. Hargrive, Bartow, President; Dr. R. L. Hughes, Bartow, Vice-President; and Dr. Herman Watson, Lakeland, Secretary-Treasurer.

Walton-Okaloosa County Medical Society has elected the following officers for 1932: Dr. R. B. Spiers, DeFuniak Springs, President; Dr. E. B. Webb, Crestview, Vice-President; and Dr. A. G. Williams, Lakewood, Secretary-Treasurer.

The Central Florida Medical Society held its semi-annual meeting recently in Gainesville and elected the following officers for 1932: Dr. W. C. Thomas, Gainesville, President; Dr. J. N. Moore, Ocala, Dr. R. E. Summitt, Eustis, Dr. George C. Tillman, Gainesville, Dr. A. P. Albritton, Wildwood, Vice-Presidents; and Dr. R. H. Williams, Eustis, Secretary-Treasurer.

The Second District Medical Society, composed of Jefferson, Leon, Wakulla, Gadsden, Liberty, and Franklin Counties, has elected the following officers for 1932: Dr. W. W. Massey, Quincy, President; Dr. B. A. Wilkinson, Tallahassee, Vice-President; and Dr. O. G. Kendrick, Tallahassee, Secretary-Treasurer.

Dr. J. P. Daniels, Pensacola, has succeeded Dr. V. R. Nobles as County Physician of Escambia County.

Dr. Robert H. McGinnis, Jacksonville, has been appointed Chairman of the Committee on Necrology and will make a formal report at the annual meeting in Sarasota.

Dr. Walter A. Weed, Lakeland, Superintendent, Morrell Memorial Hospital, has been made President-Elect of the Florida Hospital Association, and Dr. Lee S. Lanpher, Duval County, Assistant Superintendent.

Dr. Louis S. Oppenheimer, Tampa, has been made an honorary life member of the Hillsborough County Medical Society, the first one ever to thus be honored.

Dr. L. S. Laffitte, Gulf Hammock, has received an appointment to residency for one year at Bellevue Hospital, New York City.

DEATHS

Dr. James L. Niblack, Lake City, aged 81, died February 7 of carcinoma of the pancreas.

Dr. Edward Thomas Craney, Orlando, aged 54, died February 22 of pneumonia.

GEORGIA

Elbert County Medical Society has elected the following officers for 1932: Dr. F. L. Adams, Elberton, President; Dr. F. A. Smith, Elberton, Vice-President; and Dr. A. S. Johnson, Elberton, Secretary-Treasurer.

Floyd County Medical Society has elected the following officers for 1932: Dr W. B. Floyd, Rome, President; Dr. R. C. Maddox, Rome, Vice-President; and Dr. Robert M. Harbin, Jr., Rome, Secretary-Treasurer.

Jefferson County Medical Society has elected the following officers for 1932: Dr. S. T. R. Revell, Louisville, President; Dr. J. J. Pilcher, Wrens, Vice-President; and Dr. S. C. Ketchin, Louisville, Secretary-Treasurer.

Richmond County Medical Society has elected the following officers for 1932: Dr. W. W. Battey, Jr., President; Dr. E. A. Wilcox, Vice-President; and Dr. Richard B. Weeks, Secretary-Treasurer; all of Augusta.

Dr. W. H. Lott, Monroe, recently took a sixty-day postgraduate course at the New York Polyclinic, resuming his practice at Monroe the first of April.

Dr. M. F. Cochran, Dr. T. S. Bailey, Dr. R. H. McDonald, and Dr. George W. Hammond, all of Newnan, have opened a joint office in Franklin for the practice of medicine.

Dr. J. H. Hines, Atlanta, has been made Superintendent of the Medical Service of the Grady Hospital.

Dr. L. G. Neal, has moved his office from Gainesville to Cleveland.

Dr. H. M. Sale has moved from Rayle to Sharon.

Dr. J. W. Clements, Gore, celebrated his ninety-first birthday with a dinner given him by members of the Chattooga County Medical Society, the Floyd County Medical Society, and other friends.

Dr. John Davidson Wiley, Milledgeville, and Miss Frances Reese were married March 17.

DEATHS

Dr. William Zellars Holliday, Atlanta, aged 72, died February 20 of arteriosclerosis.

Dr. William Richard Bulgin, Cleveland, aged 64, died December 17, 1931, of cerebral hemorrhage.

Dr. LaFayette Alonza Carter, Nashville, aged 73, died February 29.

Dr. Malcolm M. Currie, Alston, aged 79, died February 12.

KENTUCKY

Lydia M. Haase is the new Superintendent of the Community Hospital at Glasgow.

Nell Conniff has been made Superintendent of Riverside Hospital at Paducah.

DEATHS

Dr. Alva M. Shupert, Louisville, aged 62, died in February.

Dr. Frank Elmer Locke, Newport, aged 71, died February 28 of chronic myocarditis.

Dr. Jefferson D. Cundiff, Drakesboro, aged 69, died February 5 of angina pectoris.

Dr. Robert Pierce Thomas, Glencoe, aged 80, died February 23 of nephritis.

Dr. James Madison Morris, Lexington, aged 58, died February 12 of heart disease.

Dr. Robert Cornelius Fleming, Louisville, aged 54, died February 12.

LOUISIANA

Dr. C. Jeff Miller, New Orleans, was the guest speaker at the Southeastern Surgical Congress held recently in Birmingham.

Dr. Charles J. Bloom, New Orleans, Professor in the Graduate School of Medicine at Tulane, gave an address before the Seventh District Medical Society at its meeting in Jennings.

Dr. Oscar W. Bethea, New Orleans was a guest speaker at the South Mississippi Medical Society meeting in Laurel.

Dr. B. L. Newell, U. S. Public Health Service, has been assigned to duty as Chief Medical Officer of the Federal Jail in New Orleans.

Mr. Edward Groner has been made Superintendent of Baptist Hospital at Alexandria.

DEATHS

Dr. James Birney Guthrie, New Orleans, aged 56, died March 8 in Touro Infirmary of heart disease.

Dr. S. C. Waller, Shreveport, aged 70, died February 1 of heart disease.

Dr. Joseph Frank Chretien, New Orleans, aged 69, died December 17, 1931.

MARYLAND

Dr. John Ruhrah, Baltimore, has been named to prepare the history of the medical profession in the State for the last twenty-five years, this appointment having been made by the Medical and Chirurgical Faculty of Maryland.

In celebrating the fiftieth anniversary of Robert Koch's announcement of his discovery of the tubercle bacillus, Baltimore had a special exhibition of books and other material relating to Robert Koch and to tuberculosis, which was held in the Welch Medical Library of the Johns Hopkins University Medical School. Dr. Henry Barton Jacobs displayed the books, and Dr. William H. Welch, Director Emeritus of the Institute of the History of Medicine, gave reminiscences of Koch.

The Dohme Lectures at the Johns Hopkins University School of Medicine were delivered in April by Professor Waldschmidt-Leitz of the Institute of Biochemistry, Prague.

Dr. Bradford Massey, Berlin, and Miss Sarah D. Snook were married March 5.

DEATHS

Dr. Germanus J. France, Baltimore, aged 42, died February 9.

Dr. Maclane Cawood, West River, aged 51, died February 29 of heart disease.

Dr. William Quail Skilling, Lonaconing, aged 72, died February 6 of pneumonia.

Dr. Helen Louise Smith, Takoma Park, aged 69, died suddenly January 21 of heart disease.

MISSISSIPPI

Dr. George T. Warren, Brookhaven, has been elected Vice-President of the Tri-County Medical Society to fill the unexpired term of Dr. R. E. Higdon, who died recently.

Dr. Roland E. Cutts, formerly of the Mayo Clinic, has located in Vicksburg and become associated with the Vicksburg Clinic, practising pediatrics.

Carra Lamb is the newly appointed Superintendent of Tupelo Hospital.

Dr. Hunter Ledbetter Scales, Starkville, and Mrs. Julia Hull Brown were married recently.

DEATHS

Dr. Chester Winfred Smith, Glendora, aged 72, died February 22 in Memphis.

Dr. Robert R. Bridges, Crystal Springs, aged 77, died February 26.

Dr. Washington La Fayette Doss, Columbus, aged 65, died January 22 in Crawford.

MISSOURI

Caldwell-Livingston County Medical Society, just recently organized, has elected the following officers for 1932: Dr. C. H. Wilbur, Polo, President; Dr. R. J. Brennan, Chillicothe, Vice-President; and Dr. Donald M. Dowell, Chillicothe, Secretary-Treasurer.

Cole County Medical Society has elected the following officers for 1932: Dr. W. A. Clark, Jefferson City, President; Dr. F. W. Gilham, Jefferson City, Vice-President; and Dr. James A. Hill, Jefferson City, Secretary-Treasurer.

Continued on page 32

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Continued from page 558

Cooper County Medical Society has elected the following officers for 1932: Dr. Alex Van Ravenswaay, Boonville, President; Dr. G. L. Chamberlain, New Franklin, Vice-President; and Dr. T. C. Beckett, Boonville, Secretary-Treasurer.

Lawrence-Stone County Medical Society has elected the following officers for 1932: Dr. H. L. Kerr, Crane, President; Dr. P. A. Holmes, Mount Vernon, Vice-President; and Dr. J. W. Smith, Verona, Secretary-Treasurer.

Stoddard County Medical Society has elected the following officers for 1932: Dr. W. C. Dieckman, Dexter, President; Dr. S. S. Davis, Dexter, Vice-President; Dr. Frank LaRue, Dexter, Secretary; and Dr. W. J. Hux, Dexter, Treasurer.

The Tri-County Medical Association of Gentry, Harrison and Worth Counties has elected the following officers for 1932: Dr. W. T. Martin, Albany, President; Dr. W. J. Harned, Bethany, Vice-President of Harrison County; Dr. J. K. Phipps, Grant City, Vice-President of Worth County; and Dr. J. A. Crockett, Stanberry, Secretary.

The new McMillan Eye, Ear, Nose and Throat Hospital of Washington University, St. Louis, has memorialized four noted physicians with tablets in the various wards. A tablet to Dr. Frederich Eno Woodruff, St. Louis was unveiled in the Woodruff Eye Clinic; one was dedicated to Dr. Greenfield Sluder at the entrance of the Sluder Clinic; one to Dr. John B. Shapleigh was unveiled in the Shapleigh Ward; and one to Dr. John F. Shoemaker was unveiled in the Shoemaker Ward.

The Association of Assistant Physicians of Missouri at a recent meeting elected the following officers: Dr. Scott P. Child, Mt. Vernon, President; Dr. Ralph Hanks, Farmington, Vice-President; and Dr. J. W. Forman, St. Joseph, Secretary.

Dr. Max Goldstein, St. Louis, has been elected President of the St. Louis unit of the newly organized National Association for the Rehabilitation of Speech.

Dr. Malvern B. Clopton, St. Louis, has been elected President of the corporation of Washington University at a recent meeting of the Board of Directors.

Dr. Jacob Geiger, St. Joseph, celebrated the anniversary of his sixtieth year in the practice of medicine with a dinner to the Buchanan County Medical Society. Dr. J. B. Reynolds, St. Joseph, who has practiced for fifty years, shared honors with Dr. Geiger.

The postgraduate course and clinical conference of the St. Louis Clinics will be held in St. Louis for two weeks during May.

The Washington University School of Medicine has opened a new radiology institute in St. Louis, the Edward Mallinckrodt Institute of Radiology.

Anna Helen Aal has been elected Superintendent of Bothwell Memorial Hospital at Sedalia.

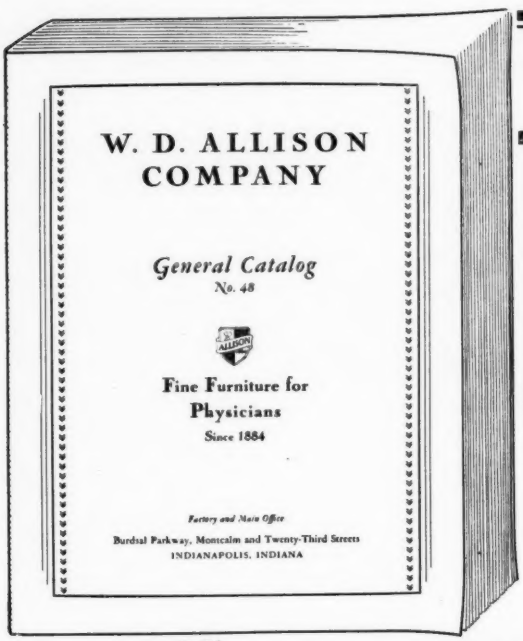
Deaths

Dr. Robert Lee Dowell, Chillicothe, aged 64, died January 30 of cerebral hemorrhage.

Dr. Charlotte Peters, St. Louis, aged 80, died January 2 from an injury received in a fall.

Dr. John William Devereux, St. Louis, aged 59, died suddenly February 15 of heart disease.

Continued on page 34



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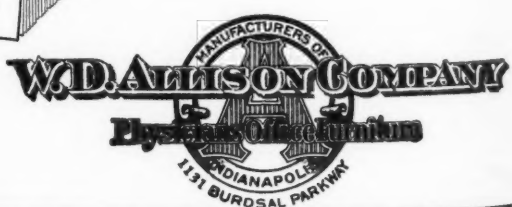

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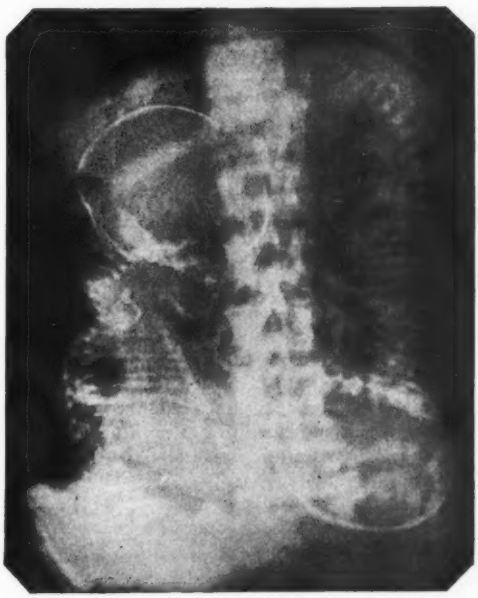

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Continued from page 32

Dr. Roy Messer Cater, Marceline, aged 50, died February 16 of nephritis.

Dr. Howard Hill, Kansas City, aged 63, died February 24 of angina pectoris.

Dr. Charles Sixtus Rehfeldt, St. Louis, aged 58, died February 13.

Dr. Zebian Headley Weyant, Kansas City, aged 59, died January 29.

Dr. Andrew Bascome Nichols, St. Louis, aged 79, died January 29.

NORTH CAROLINA

The Durham-Orange County Medical Society had as their guest speaker at a recent meeting at the Duke Hospital, Dr. George R. Minot, of Harvard Medical School, Boston.

The Duke University School of Medicine and Duke Hospital recently sponsored a clinic on cancer of the breast conducted by Dr. Joseph Colt Bloodgood of Johns Hopkins University School of Medicine, Baltimore.

Ruth Bean has been made Superintendent of Biltmore Hospital, Asheville.

Dr. Lester Avant Crowell, Jr., Lincolnton, and Miss Elaine Deal were married March 24.

DEATHS

Dr. Charles Mortimer Montgomery, Oteen, aged 55, died March 3 of chronic pulmonary tuberculosis.

OKLAHOMA

DEATHS

Dr. Wilber Elmer Rammell, Bartlesville, aged 70, died March 15 of carcinoma of the larynx.

Dr. Calvin J. K. Moore, Thomas, aged 71, died February 21 of nephritis.

Dr. Robert Calhoun Caldwell, Bradley, aged 80, died January 21.

Dr. Benjamin F. Hamilton, Shawnee, aged 74, died February 12.

SOUTH CAROLINA

Dr. Sam Harry Ross, Jr., Seneca, and Miss Edna Aileen Tollison were married March 5.

DEATHS

Dr. Hawkins Whitworth Corbett, Anderson, aged 42, died February 27 of pneumonia.

Dr. Theodore Edward Percival, Greenwood, aged 30, died December 28.

Dr. Jacob Paul Stroman, McClellanville, aged 68, died January 30 of heart disease.

Dr. John Martin Weekley, Ulmer, aged 94, died January 25.

Dr. David H. Funderburk, Lancaster, aged 66, died December 4, 1931.

TENNESSEE

Dr. Eugene Rosamond, Memphis, has been appointed the member of the Council from Tennessee of the Southern Medical Association, the appointment having been announced recently by the President, Dr. Lewis J. Moorman, Oklahoma City, Oklahoma. Dr. Rosamond succeeds Dr. Edward T. Newell, Chattanooga, whose term had expired, and who, having served the constitutional limit, was not eligible to reappointment.

Dr. John L. Jelks, Memphis, and Dr. Victor K. Allen, Tulsa, will be in charge of arrangements for the meeting of the American Proctologic Society in Memphis May 6 and 7.

A joint meeting of the Kentucky, Tennessee and Arkansas Hospital Association was held in Memphis in April. Superintendents of hospitals in Alabama and Georgia were invited to attend.

The West Tennessee Medical and Surgical Association will meet in Jackson May 26 and 27, with Dr. Sam T. Parker, Jackson, President of the Association, and Dr. I. A. McSwain, Paris, Secretary.

Dr. Joseph Travenick, Jr., Nashville, has opened offices in the

Continued on page 36

Mothers do not forget to give babies their feedings, though they easily might neglect to give them an added antirachitic agent.

"Clinical study reveals a high antirachitic potency. DRYCO produces definite healing in cases of moderate infantile rickets."
(Report of Committee on Foods of the American Medical Association, J.A.M.A., Vol. 98, No. 1, p. 49, Jan. 2, 1932.

Build Your Baby Patients' Resistance to Summer Troubles Through Their Food—IRRADIATED DRYCO

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DRYCO

Made from superior quality milk from which part of the butterfat has been removed, irradiated by the ultraviolet ray, under license by the Wisconsin Alumni Research Foundation (U. S. Patent No. 1,680,818) and then dried by the "Just" Roller Process.

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ALL DRYCO IN THE HANDS OF DRUGGISTS IS IRRADIATED

A Dependable Source of Blood-Building Iron

PHYSICIANS realize that iron for blood building must be in an easily assimilable form associated with other mineral substances. They also know that many anemic patients cannot tolerate the large amount of spinach or other greens necessary to supply the iron requirements.

A better method must be found for increasing the intake of usable iron and that method is now offered in an iron concentrate —

FOOD FERRIN

Food Ferrin contains an abundance of soluble iron associated with copper, the chlorophyll of plants and in such concentrated form that a tablespoonful — the usual dose — supplies as much iron as a pound of spinach.

Not only is Food Ferrin more effective than the usual iron tonics, but it is more acceptable — it has an agreeable taste, does not disturb digestion, does not injure the teeth nor cause constipation.

For test purposes we will gladly send you a physician's sample of Food Ferrin with our compliments.

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Send me, without obligation, literature and trial bottle of Food Ferrin.

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Address .....

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Continued from page 34

Bennie-Dillon Building for the practice of urology and urological surgery.

Dr. A. B. Dancy, Jackson, was elected President-Elect of the Mid-South Post Graduate Medical Assembly at the last annual meeting in Memphis.

Dr. R. A. Douglas, Huntington, is erecting an office next to Hotel Olive.

Dr. J. S. Lyons, Rogersville, has resumed his practice after completing a course in surgery in Chicago and Rochester.

Dr. J. Ralph Hamilton, formerly of Dallas, Texas, has located in Knoxville where he is associated with Dr. H. E. Christenberry.

Dr. Edward H. Barksdale, Nashville, and Miss Louise Paty were married March 5.

Deaths

Dr. Elizabeth C. Kane, Memphis, aged 55, died February 10 in a hospital in Baltimore of carcinoma of the colon.

Dr. William Herman Stone, Wilder, aged 45, died February 8 of heart disease.

Dr. James Martin Rippey, Union City, aged 73, died January 22.

Dr. Claude M. Kelton, Fort Lyon, aged 55, died February 18.

TEXAS

Bell County Medical Society has elected the following officers for 1932: Dr. M. W. Sherwood, President; Dr. W. J. Graber, Jr., Vice-President; and Dr. R. K. Harlan, Secretary-Treasurer; all of Temple.

Denton County Medical Society has elected the following officers for 1932: Dr. M. L. Holland, President; Dr. J. H. Hicks, Vice-President; and Dr. L. O. Hayes, Secretary-Treasurer; all of Denton.

Fannin County Medical Society has elected the following officers for 1932: Dr. C. A. Gray, President; Dr. D. J. Saunders, Vice-President; and Dr. A. B. Kennedy, Secretary-Treasurer; all of Bonham.

Karnes-Wilson Counties Medical Society has reelected all of last year's officers for 1932, as follows: Dr. J. W. Oxford, Floresville, President; Dr. W. F. Hickle, Kennedy, Vice-President; and Dr. R. C. Youngblood, Falls City, Secretary-Treasurer.

Wood County Medical Society has elected the following officers for 1932: Dr. V. E. Robbins, Quitman, President; Dr. T. B. Reed, Mineola, reelected Vice-President; and Dr. W. T. Black, Quitman, Secretary-Treasurer.

The Seventh District Medical Society met in Austin and elected the following officers for 1932: Dr. Truman N. Morris, Austin, President; Dr. J. W. Jackson, Austin, Vice-President; and Dr. H. C. Perkins, Austin, Secretary-Treasurer.

Dr. D. H. Hudgins, and Dr. P. C. Shands, both of Forney, have been made co-managers of the Forney Sanitarium.

Dr. W. H. Brandau, Beaumont, was elected President of the Beaumont General Hospital Staff.

Dr. A. I. Folsom, Dallas, has been elected Chairman of the Staff of the Baylor Hospital.

Dr. J. Frank Clark, Abilene, is the newly elected President of the West Texas Baptist Hospital.

Dr. J. R. Gillam, Mart, has been made President of the Chamber of Commerce of Mart.

Annyce Wallace, has succeeded Marie Tucker, resigned, as Superintendent of the Fort Worth-Tarrant County Tuberculosis Hospital at Fort Worth.

Deaths

Dr. John H. Bailey, Clyde, aged 61, died February 13 of injuries received in an automobile accident.

Dr. Albert Ferdinand Beddoe, Dallas, aged 78, died January 27.

Dr. Patrick H. Stafford, Grapeland, aged 53, died January 31 of pneumonia.

Dr. William A. Jennings, Chico, aged 57, died February 12 of cerebral embolism.

Dr. Edward Elmore Davis, Dallas, aged 69, died February 21 of acute dilatation of the heart.

Dr. Joseph Arnald Denman, Brackettville, aged 59, died February 12 of heart disease.

Continued on page 38

Klim has Always been a "Soft-Curd" Milk

RECENT scientific literature has stressed the advantages of soft-curd milks in infant feeding. (*Hill, R. L.: Archives of Pediatrics, July 1931, XLVIII:417*)

When you prescribe Klim, the powdered whole milk, you prescribe a soft-curd milk, because the casein of this standard dried milk is finely divided and its butter-fat is present in small particles. This, of course, is the natural result of the Merrell-Soule spray process of dehydration.

The Klim curd therefore more closely resembles mother's milk, in its characteristics, than does the average fluid milk. In infant feeding Klim promotes digestion and assures a higher degree of assimilation. Recent impartial investigations confirm this fact.

● "*Klim showed the highest apparent digestibility—indeed the drying has rather the tendency of increasing the digestibility in certain cases.*"

Miyawaki et al. Jour. Dai. Sci., Jan. 1932, XV:62.

Literature and samples on request

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From the youngest to the oldest

Horlick's **The Original** Malted Milk offers a nutritious, easily digested diet.

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4. In weakened digestion
5. For sleeplessness
6. For the sick
7. In convalescence
8. As a light luncheon for all ages.

HORLICK'S, Racine, Wis.

Continued from page 36

Dr. James W. Hensley, Dewville, aged 67, died December 27, 1931.

Dr. John Thomas Scott, Dalhart, aged 68, died November 13.

Dr. Lewis Krams Beck, San Antonio, aged 53, died suddenly December 22, 1931.

Dr. John Lawson Felder, San Antonio, aged 49, died January 16.

Dr. Thomas Martin Hays, Santa Anna, aged 66, died January 18 of heart disease.

VIRGINIA

The Post-Graduate Medical Society of Southern Virginia held its annual meeting at Lawrenceville recently and elected the following officers for 1932: Dr. W. W. Seward, Surry, President; Dr. H. C. Stoneham, Waverly, Dr. E. L. Kendig, Victoria, Vice-Presidents; and Dr. Philip Jacobson, Petersburg, Secretary-Treasurer.

Accomack Medical Society has elected the following officers for 1932: Dr. James C. Doughty, Onancock, President; Dr. Ira Hurst, Parksley, Vice-President; and Dr. John W. Robertson, Onancock, Secretary-Treasurer.

The Gill Memorial Hospital of Roanoke recently had as their guest Dr. Edward H. Cary, Dallas, President-Elect of the American Medical Association. Dr. Cary addressed the members of the postgraduate class of the Gill Memorial Hospital and the physicians of that community.

Tazewell County Medical Society has elected the following officers for 932: Dr. J. W. Shawver, Richards, President; and Dr. Isaac Peirce, Tazewell, Secretary.

The Virginia Society of Oto-Laryngology and Ophthalmology will hold its meeting at Virginia Beach in May. Dr. Clarence Porter Jones, Newport News, is President; Dr. Courtney Edmond, Clifton Forge, Vice-President; and Dr. H. Grant Preston, Harrisonburg, Secretary-Treasurer.

Dr. A. S. Lilly has resumed his practice in Richmond after a

Continued on page 40

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Of
BLOOD DISEASES
AND INFECTION

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We supply for this purpose:

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Each season brings its own problems and the approach of hot weather reminds the physicians that infant enterocolitis may soon be expected.

For many years, Southern physicians have prescribed our Cultures in these cases with gratifying results.

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CULTURE (B. A. CULTURE)
are readily available at our depository stores throughout the South.

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In your next burn case . .

Keep the dressing wet with full-strength solution

use this Remarkable Antiseptic Dressing

HEXYLRESORCINOL SOLUTION S. T. 37 is especially indicated in the treatment of Burns and Scalds. It is germicidal and soothing.

The technic is simple: Cover the affected area with a thin layer of absorbent cotton or gauze saturated with Hexylresorcinol Solution S. T. 37, and bandage lightly to keep it in place. Keep the dressing wet with full-strength solution.

In a short time the pain and burning will subside. Leave the dressing on for 24 hours. Then note how dry, clean and relatively *insensitive* the affected area has become.

Continue the use of the wet dressings until healing starts... usually two or three days. Then use dry dressings, simply moistening the denuded area with Hexylresorcinol Solution S. T. 37 daily to prevent infection.

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The value of Gomenol Capsules in the treatment of diseases of the air passages is now definitely established!

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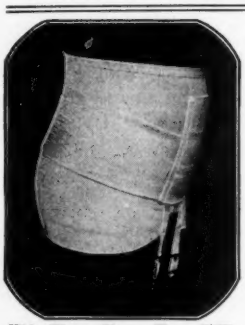
Binder and Abdominal Supporter



Gives perfect uplift and is worn with comfort. Made of Cotton, Linen or Silk, washable as underwear.

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Each Belt Made to Order **Ask for Literature**

KATHERINE L. STORM, M. D.
Originator, Owner and Maker
1701 Diamond St. **Philadelphia**

Continued from page 38

two years' absence for study, limiting his work to internal medicine.

Dr. George H. Snead, Richmond, is taking a course of study at the University of Vienna.

Dr. Benjamin E. Hunt has located temporarily at Jeffs for the practice of medicine.

Dr. W. H. Batte, formerly of Penns Grove, New Jersey, has located at Williamson and is connected with the medical staff of the Norfolk and Western Railway.

Dr. Lulu Woods Garst has resumed her work at Catawba Sanatorium after an absence in Baltimore, where she was taking special work in gastroenterology.

Dr. James Alfred Gooch and Miss Lelie Watkins Stacy, both of Richmond, were married in January.

DEATHS

Dr. James H. A. Lofland, Melfa, aged 82, died February 29 of injuries received in a fall.

Dr. Edward S. Hart, Bedford, aged 83, died February 29.

WEST VIRGINIA

Harrison County Medical Society has elected the following officers for 1932: Dr. J. F. Williams, President; Dr. Harry H. Esker, Vice-President; Dr. Joe R. Carder, Secretary; and Dr. Robert C. Hood, Treasurer; all of Clarksburg.

Lincoln-Boone Counties Medical Society, just recently organized, has elected the following officers for 1932: Dr. J. C. Kessler, Hamlin, President; Dr. A. J. Hatfield, Madison, Vice-President; Dr. George W. Walden, West Hamlin, Treasurer; and Dr. H. H. Howell, Madison, Secretary.

Preston County Medical Society has elected the following officers for 1932: Dr. Harold Miller, Eglon, President; Dr. E. D. Wise, Rowlesburg, Vice-President; and Dr. F. D. Fortney, Hopemont, Secretary-Treasurer.

Summers County Medical Society reports a 100 per cent paid up membership for 1932.

DEATHS

Dr. Joseph Edward Rader, Huntington, aged 60, died February 26.

Dr. Elbert F. Peters, Princeton, aged 54, died February 29.

Classified Advertisements

YOUNG SURGEON wishes part-time pathological appointment. Mayo training both branches. Interview at A.M.A. convention. Address L. P. W., care Journal.

YOUNG DOCTOR, aged 38, several years' experience, desires location to act as assistant in surgery. Can give good references. Have had some training in the East, following graduation in middle West. Salary or percentage basis. Available April 1 Address B. B. K., care Journal.

TECHNICIAN—Thoroughly trained laboratory technician with an A.B. degree from a Southern college desires position. Three years in hospital as technician; can furnish best of references. Address W. A., care Journal.

ASSISTANCE OFFERED TO MEDICAL WRITERS. Research. Abstracts. Translations (all languages). Papers prepared from author's data. Ten years' experience with leading physicians and appointments on medical journals of highest standing. I employ no assistants; all my work is done personally and is reliable. Florence Annan Carpenter, 413 St. James Place, Chicago, Ill.

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TIME TELLS!

In the last twenty years in America every so often some new form of anesthetic has been put on the market, sometimes with most startling claims. Most of them vanish as rapidly as they come, because they cannot stand the test of time.

It was just about twenty years ago that NITROUS OXID AND OXYGEN first came into real use as a major anesthetic. Today, supplemented by ETHYLENE and CARBON DIOXID gases, they are more largely consumed than ever before, and the consumption is constantly growing. THE USE OF THESE PRODUCTS HAS STOOD THE TEST OF TIME.

Back of the Puritan Maid Label on each and every cylinder identifying the products of the Puritan Compressed Gas Corporation is the reputation of eighteen years in the field. For safety reasons we differentiate our gases with distinctive colors over the entire cylinder, as recommended by the resolution of the International Anesthesia Research Society.

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Insure potency and constancy of action by prescribing the products of

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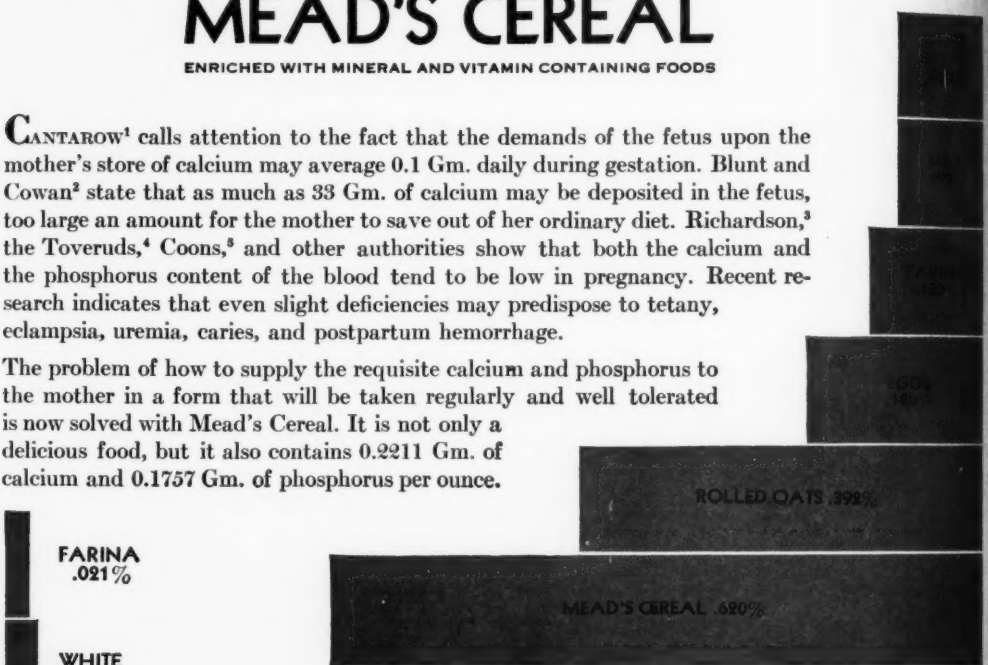
In PREGNANCY—Calcium Therapy in Food Form

MEAD'S CEREAL

ENRICHED WITH MINERAL AND VITAMIN CONTAINING FOODS

CANTAROW[1] calls attention to the fact that the demands of the fetus upon the mother's store of calcium may average 0.1 Gm. daily during gestation. Blunt and Cowan[2] state that as much as 33 Gm. of calcium may be deposited in the fetus, too large an amount for the mother to save out of her ordinary diet. Richardson,[3] the Toveruds,[4] Coons,[5] and other authorities show that both the calcium and the phosphorus content of the blood tend to be low in pregnancy. Recent research indicates that even slight deficiencies may predispose to tetany, eclampsia, uremia, caries, and postpartum hemorrhage.

The problem of how to supply the requisite calcium and phosphorus to the mother in a form that will be taken regularly and well tolerated is now solved with Mead's Cereal. It is not only a delicious food, but it also contains 0.2211 Gm. of calcium and 0.1757 Gm. of phosphorus per ounce.



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MEAD'S CEREAL Supplies Calcium; MEAD'S VIOSTEROL Utilizes Calcium

Mead's Cereal added to the usual daily diet of the expectant mother will in most cases supply all the calcium and phosphorus required. In a serving of 4 ounces* the patient receives the minimum daily requirement (0.45 Gm. Ca and 0.68 Gm. P)[6] from this one food alone. And when Mead's Viosterol is also administered during the prenatal period, it becomes possible for the patient to utilize these minerals more fully. Thus by correcting calcium-phosphorus imbalance, the toxemias of pregnancy and the danger of hemorrhage can be minimized.

1—6 Bibliography on request

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CANTAROW[1] calls attention to the fact that the demands of the fetus upon the mother's store of calcium may average 0.1 Gm. daily during gestation. Blunt and Cowan[2] state that as much as 33 Gm. of calcium may be deposited in the fetus, too large an amount for the mother to save out of her ordinary diet. Richardson,[3] the Toveruds,[4] Coons,[5] and other authorities show that both the calcium and the phosphorus content of the blood tend to be low in pregnancy. Recent research indicates that even slight deficiencies may predispose to tetany, eclampsia, uremia, caries, and postpartum hemorrhage.

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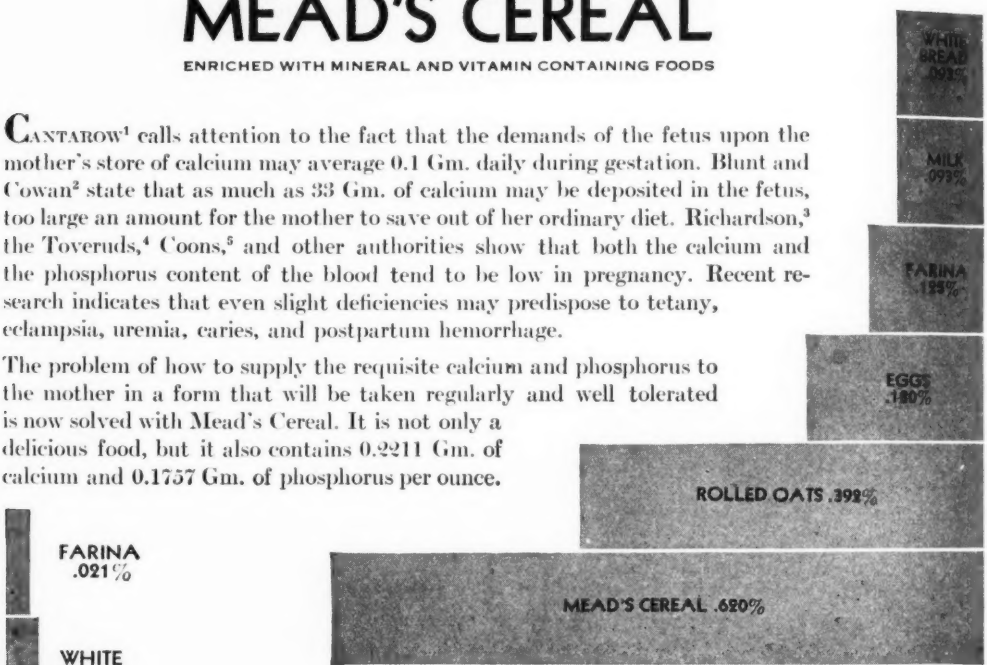

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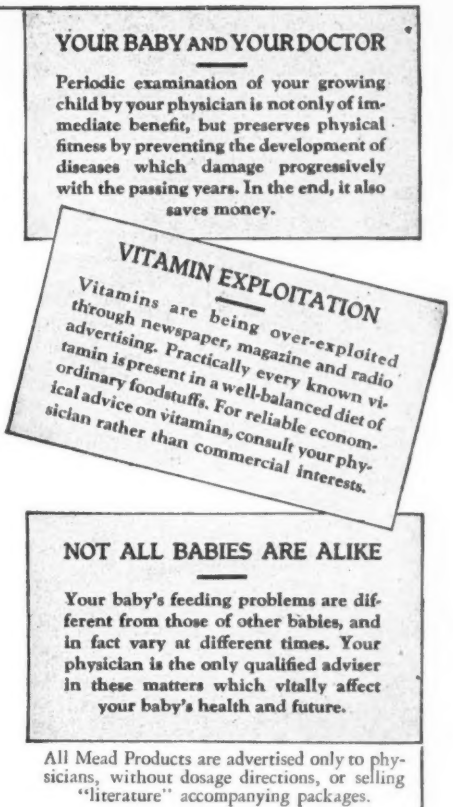
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Periodic examination of your growing child by your physician is not only of immediate benefit, but preserves physical fitness by preventing the development of diseases which damage progressively with the passing years. In the end, it also saves money.
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